COMPARATIVE EVALUATION OF BONE REGENERATION AFTER SURGICAL REMOVAL OF IMPACTED MANDIBULAR THIRD MOLARS USING HYDROXYAPATITE WITH AND WITHOUT PLATELET RICH FIBRIN

A Dissertation submitted in

partial fulfillment of the requirements for the degree of

MASTER OF DENTAL SURGERY

BRANCH – III

ORAL AND MAXILLOFACIAL SURGERY

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI – 600 032

2013 - 2016

ENDORSEMENT BY HEAD OF THE DEPARTMENT /

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This is to certify that the Dissertation entitled "**COMPARATIVE EVALUATION OF BONE REGENERATION AFTER SURGICAL REMOVAL OF IMPACTED MANDIBULAR THIRD MOLARS USING HYDROXYAPATITE WITH AND WITHOUT PLATELET RICH FIBRIN**" is a bonafide work done by **Dr. ISHA KOCHAR**, Post Graduate student (2013-2016) in the Department of Oral and Maxillofacial Surgery, under the guidance of **Dr. B. SARAVANAN, M.D.S., Ph.D.,** Professor, Department of Oral and Maxillofacial Surgery, Tamil Nadu Government Dental College and Hospital, Chennai – 600 003.

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This is to certify that **Dr. ISHA KOCHAR**, Post Graduate student (2013-2016) in the Department of Oral and Maxillofacial Surgery, Tamil Nadu Government Dental College and Hospital, Chennai – 600 003 has done this dissertation titled **"COMPARATIVE EVALUATION OF BONE REGENERATION AFTER SURGICAL REMOVAL OF IMPACTED MANDIBULAR THIRD MOLARS USING HYDROXYAPATITE WITH AND WITHOUT PLATELET RICH FIBRIN"** under my direct guidance and supervision in partial fulfillment of the regulations laid down by **The Tamil Nadu Dr. M.G.R. Medical University,** Chennai – 600 032 for **Master of Dental Surgery**, Oral and Maxillofacial Surgery (Branch III) Degree Examination.

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation titled **"COMPARATIVE EVALUATION OF BONE REGENERATION AFTER SURGICAL REMOVAL OF IMPACTED MANDIBULAR THIRD MOLARS USING HYDROXYAPATITE WITH AND WITHOUT PLATELET RICH FIBRIN"** is a bonafide and genuine research work carried out by me under the guidance of **Prof. Dr. B. SARAVANAN, M.D.S., Ph.D., Professor,** Department of Oral and Maxillofacial Surgery, Tamil Nadu Government Dental College and Hospital, Chennai - 600003**.**

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Signature of the candidate

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And

Dr. ISHA KOCHAR, aged 28 years currently studying as final year **Post Graduate student** in the Department of Oral and Maxillofacial Surgery, Tamil Nadu Government Dental College and Hospital, Chennai -3 residing at Kellys, Chennai. (hereafter referred to as the 'PG and co- investigator')

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Principal

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Witnesses

1.

2.

ACKNOWLEDGEMENT

With immense gratitude, I thank my esteemed Guide and Principal, **Dr. B.Saravanan, M.D.S., Ph.D.,** Professor, Department of Oral & Maxillofacial Surgery, Tamil Nadu Government Dental College and Hospital for his relentless encouragement, support and guidance in successfully completing the study. His never ending patience and affable personality has been a source of encouragement throughout my post graduate period. His meticulous and systematic way of providing constructive viewpoints has inspired my entire approach towards the subject and its practice.

I offer with profound respect and my heartfelt thanks to **Dr. P. Srimathi, M.D.S,** Professor and HOD, Department of Oral & Maxillofacial Surgery for her unrestricted help, valuable guidance and advice throughout the post graduate period.

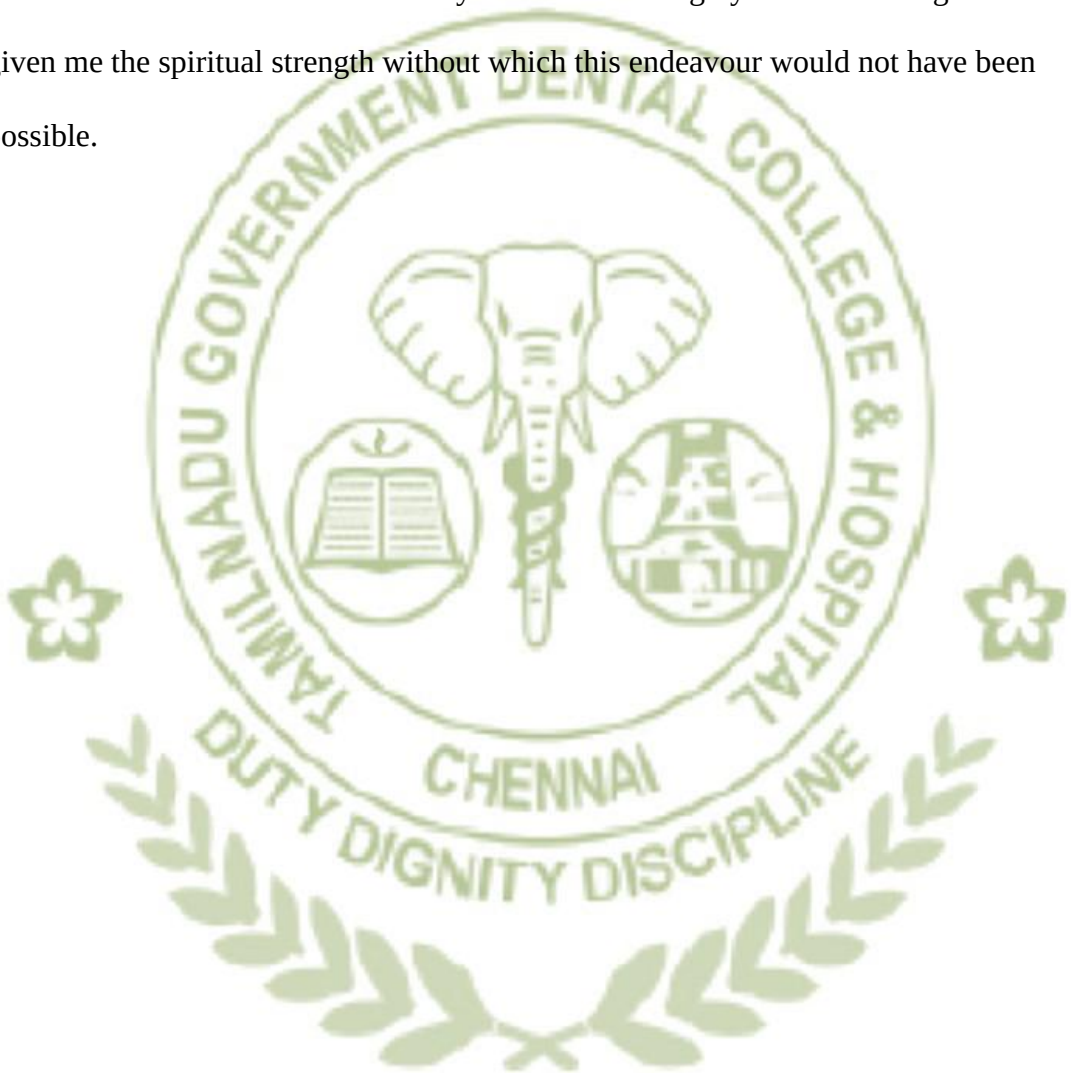
I express my sincere thanks to **Dr. D. Durairaj, M.D.S. and Dr. C. Prasad, M.D.S.,** Professors, Department of Oral and Maxillofacial Surgery, for their encouragement and guidance, throughout my post-graduation period.

I extend my sincere thanks to my co-guides **Dr. J. Balaji, M.D.S,** Associate Professor and **Dr. M. Arulmozhi, M.D.S,** Assistant professor.

I express my special thanks to all other Associate Professors and Assistant professors of my department for their encouragement and timely help during the course of study.

I dedicate this study to my parents for their unwavering support in all my endeavours. Any accomplishment in my life would not be possible without their constant love and prayers. I also offer my heartfelt thanks to my friends for their moral support.

Last but not the least I humbly bow to the Almighty whose blessings have given me the spiritual strength without which this endeavour would not have been possible.



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APPROVAL FROM INSTITUTIONAL ETHICS COMMITTEE TO PROCEED WITH THE RESEARCH WORK

Title of the work: Comparative evaluation of bone regeneration after surgical removal of impacted mandibular third molars using hydroxyapatite with and without platelet rich fibrin

Principal Investigator: Dr.Isha Kochar
II year , MDS

Department : Department of Oral and Maxillofacial surgery
Tamil Nadu Govt. Dental College & Hospital , Chennai-3

Thank you for submitting your research proposal , which was considered at the Institutional Ethics Committee meeting(IEC) held on the 6th. February 2015, at TN Govt. Dental College and the documents related to the study referred above were discussed and the modifications done as suggested and reported to us through your letter dated 07-05-2015 have been reviewed.

The decision of the members of the committee , the secretary and the Chairperson IEC of TN Govt. Dental College is here under:

Approved	Approved and advised to proceed with the study
Approved with suggestions	----------
Revision	----------
Rejected	----------

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ABSTRACT

BACKGROUND: Platelet-Rich Fibrin (PRF) is a new second-generation platelet concentrate, with simplified processing, and no biochemical blood handling. It is a natural bioactive membrane, which can enhance soft/hard tissue healing, at the same time, can also protect surgical sites and grafted materials from external aggressions. The purpose of this study is to compare the efficacy of platelet-rich fibrin in regeneration of bone when mixed with porous hydroxyapatite and grafted in mandibular third molar socket with that of plain hydroxyapatite (without PRF), with a follow up period of 6 months.

MATERIALS AND METHODS: A total of 30 patients divided into 3 groups (10 patients in each group); both male and female, aged between 17 and 45 years, who had impacted mandibular third molars with similar anatomical position were randomly selected for this study. The evaluation of osseous regeneration by trabecular pattern assessment was done for a period of six months. Bone density was calculated at the end of six months.

RESULTS: An increase in bone density was observed in the PRF with hydroxyapatite group (Group I) compared to hydroxyapatite (Group II) and control groups (Group III).

CONCLUSION: Definitive improvement in initiation and acceleration of hard tissue healing was seen along with increase in bone density in the PRF with hydroxyapatite group (Group I).

KEY WORDS: Impacted mandibular third molar, Hydroxyapatite, Platelet rich fibrin, Bone density, Computed tomography scan

LIST OF ABBREVIATIONS

ANOVA	Analysis of Variance
BMP	Bone morphogenic protein
B-TCP	β- Tricalcium phosphate
CT	Computed tomography
DBM	Demineralized bone matrix
ECM	Extracellular matrix
FDBA	Freeze dried bone allograft
HA	Hydroxyapatite
IGF	Insulin-like growth factor
IL-1	Interleukin-1
OPG	Orthopantomogram
PDGF	Platelet derived growth factor
PPP	Platelet poor plasma
PRF	Platelet rich fibrin
PRP	Platelet rich plasma
VAS	Visual analog scale
VEGF	Vascular endothelial growth factor

CONTENTS

INTRODUCTION

Bone is a specialized form of connective tissue that provides support and protection for vital structures. The replacement of diseased, injured or worn parts of bone has been a dream of man for many years. Bone regeneration is a complex, well-orchestrated physiological process of bone formation, which can be seen during normal fracture healing, and is involved in continuous remodelling throughout adult life.

Even though bone has a good healing capacity compared to other tissues, the regeneration potential is limited in the case of large defects such as after tumor resection, major fractures, hip implant revision or impaired healing capacity of the host. It has been shown that after tooth extraction, the surrounding jawbone tends to recede and atrophy, eventually losing nearly 40% - 60% of its original height and width within 2-3 years. This atrophy occurs regardless of the patient's age, sex or teeth. Socket grafting or ridge preservation is the immediate treatment for replacement of extracted tooth or teeth. In such cases, the use of bone grafts, derivates or bone substitutes are indicated to promote healing and regeneration.

The presence of impacted mandibular third molars has been shown to increase the risk of angle fractures. This increased risk is related to the decreased amount of bone, resulting in a reduced resistance to traumatic forces. After removal of such teeth, placement of a bone graft improves the healing capacity of bone, thereby restoring the original height of the mandible, making it less susceptible to fracture post trauma.

The ideal bone graft or bone graft substitute should provide three essential elements:

(1) osteoconductive matrix;

(2) osteoinductive properties or factors; and

(3) osteogenic cells.

Osteoconductivity can be defined as the process of infiltration of capillaries, perivascular tissue, and osteoprogenitor cells from the host bed into the transplant.

Osteoinduction is the stimulation of a tissue to produce osteogenic elements. This process is controlled primarily by growth factors such as bone morphogenetic proteins (BMPs) that are capable of inducing differentiation of mesenchymal cells into cartilage and bone producing cells.

Osteogenic cells are mesenchymal-type cells, and they can be summoned from host or graft bone marrow.

Autogenous fresh cancellous and cortical bone (vascularized vs nonvascularized) grafts are most often used, but other graft materials include allogenic fresh frozen, freeze-dried, or processed cortical, corticocancellous, and cancellous grafts. Synthetic or engineered bone graft substitutes are the latest addition of materials.

The autogenous cancellous bone graft satisfies all three categories most completely and is considered the "gold standard" of bone transplantation.

Autogenous bone grafts have a number of advantages such as the absence of rejection and disease transmission, histocompatibility, and they retain viable osteoblasts that participate in the formation of bone. However a number of disadvantages were described: lack of sufficient transplantable materials, morbidity in the donor site, as well as the occasional need for more than one

surgical field. In addition, graft survival is unpredictable and its resorption cannot be foretold.

It is for the reason that in recent years several biocompatible materials have emerged as substitutes of autogenous bone. These can be classified into two major groups: organic and synthetic. Hydroxyapatite [Ca_{10} $(PO_4)_6$ $(OH)_2$] is a synthetic biomaterial. Porous hydroxyapatite has an excellent bone conductive property which permits the growth of osteogenic cells from existing bone surfaces into adjacent bone graft material. Studies have shown that hydroxyapatite is well tolerated by the surrounding tissues with no evidence of inflammation and is appropriate for application in humans.

Developed in France by **Choukroun et al.**[1] in 2001, Platelet-rich fibrin (PRF) is a second-generation platelet derivative because, unlike other platelet concentrates like platelet-rich plasma (PRP), this technique does not require anticoagulants nor bovine thrombin or any other gelifying agent. PRF is an immune and platelet concentrate which is obtained on a single fibrin membrane, containing all the constituents of a blood sample which are favourable for healing and immunity. It consists of a fibrin matrix polymerized in a tetra molecular structure, with incorporation of platelets, leucocytes, cytokines, and circulating stem cells. Clinical studies reveal that this biomaterial would be a favourable matrix for the development of a coherent healing, without any inflammatory excess.

Due to its mechanical function and a rapid angiogenesis promoting ability, PRF membranes are viable material for all types of superficial cutaneous and mucosal healing. PRF in the form of a platelet gel can be used in conjunction with bone grafts, which has several advantages, such as promoting wound healing,

bone growth and maturation, wound sealing and hemostasis, and imparting better handling properties to graft materials.

The purpose of this prospective clinical study is to evaluate the osseous regeneration potential of PRF mixed with porous hydroxyapatite when grafted in extraction socket after surgical removal of impacted mandibular third molars.

AIM

The purpose of this study is to compare the efficacy of platelet-rich fibrin in regeneration of bone when mixed with porous hydroxyapatite and grafted in mandibular third molar socket with that of plain hydroxyapatite (without PRF), with a follow up period of 6 months.

OBJECTIVES

1. To compare mandibular bone regeneration by placing platelet-rich fibrin (PRF) with hydroxyapatite (HA) and hydroxyapatite (HA) alone with control group over a period of six months and thus establish the potential benefits of PRF and HA in the regeneration of post-extraction alveolar bone,

2. To identify which of them, PRF mixed with HA or plain HA accelerates more bone healing and,

3. To determine whether there are differences in the postoperative symptoms (pain, trismus) in the three groups.

REVIEW OF LITERATURE

BONE REGENERATION AND REPAIR

Ollier et al. (1867) reported that the transplanted periosteum and bone remain alive and could under proper circumstances become osteogenic. He believed that viable bone with attached periosteum was the best form of graft to use.

(Barth et al, 1896) claimed that all transplanted bone marrow and periosteum die, and are replaced by surrounding tissue. He and Marchand was the first to use the term "Creeping substitution" to describe the invasion of old bone by bud like masses of new bone, with resorption of old bone.

BONE GRAFTING

Kazanjian et al. (1952) articulated four clinical rules for bone grafting situations:

1) The recipient site must have adequate blood supply which is essential to ensure the survival of any live cells on the surface of the graft.
2) Bone to bone contact must be established between the graft and the bone. This obviously facilitates "creeping substitution".
3) Rigid fixation of the fragments must be maintained during the healing period.
4) The bone graft should be placed inside the healthy tissue. A bacterially contaminated tissue bed precludes successful grafting.

(Urist and Strates, 1965) showed that a process mimicking embryonic bone formation was induced by implantation of demineralized bone into muscle.

Kusiak et al (1985), found that in membranous bone grafts, the time for revascularization was shorter than that in endochondral bone grafts and was interpreted as a factor that explained the greater resorption in endochondral bone.

(Becker, Becker, & Caffesse, 1994) used DFDBA and autogenous bone grafts to test the bone forming capacity in extraction sockets and reported that DFDBA does not induce bone formation and the material is not osteoinductive.

(Skoglund, Hising, & Young, 1996) used bio-oss in combination with a fibrinogen-thrombin complex as grafting material prior to implant placement in humans and found that xenograft will act similarly to the host bone, which often undergoes remodeling at a very slow rate.

IDEAL REQUIREMENT OF THE BONE GRAFTS:

Schullhorn et al. (1996) put forward ideal requirements for a bone graft material:

1) Biologic acceptability.
2) Predictability.
3) Clinical feasibility.
4) Minimal operative hazards.
5) Minimal post-operative sequelae.
6) Patient acceptance.

HYDROXYAPATITE GRAFT

(Sapkos et al, 1986) implanted hydroxyapatite around teeth which were destined to go for extraction with the objective of histologically assessing the

material and the results showed that hydroxyapatite was well tolerated by the surrounding tissues with no evidence of inflammation.

(Donath, Rohrer, & Beck-Mannagetta, 1987) noted dissolution of some particles with granules of hydroxyapatite present within the cytoplasm of macrophages by augmenting dense hydroxyapatite in a segment of resected mandible and the study showed the presence of bone between the particles.

(Holmes, Wardrop, & Wolford, 1988) used porous hydroxyapatite as a bone graft substitute in mandibular contour augmentation. All grafts become increasingly resorbed with time whereas all implants remained intact and porous hydroxyapatite matrix demonstrated long term permanence with maintenance of contour and also studied the use of porous hydroxyapatite as a substitute for bone in grafting associated with orthognathic surgical procedure, and the biologic response to hydroxyapatite matrix confirmed its ability to serve as a bone graft substitute in clinical applications.

Lang et al (1989) conducted a comparative test of the soluble toxicity of hydroxyapatite ceramics using human and animal osteoblasts and demonstrated that the osteoblast-like cell cultures are a highly sensitive test system for materials with low toxicity.

(Bucholz, Carlton, & Holmes, 1989) implanted autograft or coralline hydroxyapatite into metaphyseal defects of 40 patients with tibial plateau fractures and found no differences between the two groups at a minimum of 15 months of follow up.

(Mehlisch, Leider, & Roberts, 1990) showed bone infiltration throughout full cores of hydroxyapatite-purified collagen of bovine extract specimens in

humans and noted that some specimens had scalloped edges, with inflammatory cells at the periphery of the augmented ridge.

(Friedman et al., 1991) showed that the osseointegrative capacity of hydroxyapatite cement is advantageous over ceramic hydroxyapatite and studies indicate that both forms lack significant fibrous encapsulation, produce a minimal inflammatory response and result in no foreign body giant cell formation, showed 63% osseous replacement within 18 months, and no toxic reactions or increase in serum calcium and phosphate levels were detected this period and he favored the term 'osteoconverison' for this type of implant, which means the substitution of the implant with new bone formation without losing a significant volume.

Yu, Wong et al (1992) showed self-setting hydroxyapatite cement as a novel skeleton drug delivery system for antibiotics to be used to treat osteomyelitis.

Wise and Merten (1993) showed the role of periosteum in osteointegration of hydroxyapatite granules. Periosteum is the ideal natural membrane to stop invasion of fibroblasts and other cells that prevent bone formation. If kept intact, new bone may proceed from the base at the bone-implant interface throughout the whole mass of biomaterials and upto the periosteal layer, independent of the severity of atrophy.

(Ingram & Bonde, 1994) experimentally showed the antibacterial effects of porous granular hydroxyapatite without clarifying its mechanism.

Gosain A. K. et al (1997) reported the use of hydroxyapatite paste to correct temporal hollowing deformities after cranial vault remodeling in a growing child.

Frankenburg et al (1998), introduced Norain CRS (Craniofacial repair system) (Norton Corporation, Cupertino, calif) as a new carbonated calcium phosphate paste in the canine distal tibia, replacing the host bone. Crystalline Norain is composed of monocalcium phosphate, monohydrate, alpha-tricalcium phosphate, and calcium carbonate, mixed with sodium phosphate solution. Within 24 hours, it reaches a final compressive strength of 55 mpa and a tensile strength of 2.1 mpa. The final strength of carbonated calcium phosphate paste is superior to that of hydroxyapatite paste.

(Burstein & Cohen, 1999) used bone source (Liebinger Corporation, Kalamazoo) as the first hydroxyapatite paste in craniofacial surgery. Bone source is a combination of tetracalcium phosphate and dicalcium phosphate that sets isothermally when mixed with a sodium phosphate solution. Paste becomes firm in approximately 20 minutes but requires 24 hours to reach its maximum compressive strength of 37mpa and a tensile strength of 20mpa.

Hobar et al (2000) popularized the use of hydroxyapatite granules by mixing them with autogenous blood and microfibrillar collagen and this enhances manipulation of the formed paste to achieve better contours and also aids in hemostasis.

(Hallman, Hedin, Sennerby, & Lundgren, 2002) evaluated the survival rate of implants in maxillary sinuses augmented with bovine hydroxyapatite and autogenous bone 6 months before implant surgery and estimated dimensional changes of the bone graft with time using a new radiographic method and concluded that these grafts show good resistance to resorption.

(Ducic et al, 2002) described the use of titanium mesh and hydroxyapatite cement constructs for the treatment of large through-and-through calvarial defects

and concluded that titanium mesh and hydroxyapatite cement cranioplasty appears to be a reasonable method for reconstruction of significant calvarial defects.

(Sari, Yavuzer, & Ayhan, 2003) used hydroxyapatite granules with a porous structure of 200um obtained in prefabricated syringes of 0.8ml in mandibular defects and results revealed establishment of desired contour without any significant volume loss and without complications.

(Tuncer, Yavuzer, & Isik, 2004) evaluated the fate of hydroxyapatite cement for cranial contouring by histological evaluation of a case and observed that hydroxyapatite incorporated within the surrounding bony structures permits secondary contouring procedures. New bone and vessel formation was also detected within the implanted material but, results were not convincing for significant ostoeconversion.

(Vivek & Sripathi Rao, 2009) studied various calcium phosphate biomaterials- hydroxyapatite and tricalcium phosphate and opined that the materials are biocompatible and have the ability to become functionally integrated with natural bone, without fibrous tissue encapsulation when placed in osseous defects. They found that porous form was better than solid hydroxyapatite, because of their ability to serve as trellis for regenerating bone.

PLATELET-RICH PLASMA AND PLATELET-RICH FIBRIN WITH OR WITHOUT BONE GRAFT MATERIAL

(Tayapongsak, O'Brien, Monteiro, & Arceo-Diaz, 1994) introduced the novel idea of adding autologous fibrin adhesive (AFA) to cancellous bone during mandibular continuity reconstructions. They identified earlier radiographic bone consolidation in 33 cases; they attributed this to enhanced osteoconduction

afforded to the osteocompetent cells in the graft by virtue of the fibrin network developed by AFA. They also reported the remarkable adhesive advantage of binding cancellous marrow particles during graft placement.

(Whitman, Berry, & Green, 1997) describes the use of platelet gel as a wound sealant and dural waterproofing agent. The advantages of platelet gel over previously described biologic sealants include safety and convenience for the patient as well as improved support for tissue healing. The presence of platelets and leukocytes in the formulation adds haemostatic and antimicrobial support and brings cytokines and growth factors to the site of surgery in a manner that would not be found in fibrin glue. Thus, platelet gel offers an immediately available surgical tool to provide wound hemostasis, lymphatic sealing, and a watertight dural closure, but perhaps more importantly, it further benefits the patient by offering a reconstructive growth factor matrix to promote wound healing.

(Man, Plosker, & Winland-Brown, 2001) presented a new technique of harvesting and preparing autologous platelet gel and autologous fibrin glue and evaluate their effectiveness in stopping capillary bleeding in the surgical flaps of patients undergoing cosmetic surgery and described an effective, safe, and simple method in obtaining autologous products to help with hemostasis and wound healing in the operating room. They introduced a compact, tabletop, automated autologous platelet concentrate system to prepare autologous platelet gel and fibrin glue and compared them with autotransfusor prepared autologous platelet gel and a commercially prepared "pool" fibrin sealant (Tisseel). Their findings suggest that both products were effective in sealing capillary bed bleeding and maintaining hemostasis during elective procedures performed in twenty patients.

(Kim et al, 2002) studied the effect of particulate dentin-plaster of Paris with and without platelet-rich plasma (PRP) on bone healing and new bone formation around titanium dental implants in a canine model. All bone defects grafted with particulate dentin-plaster of Paris material showed complete healing with bone-fill. The nongrafted defects demonstrated bone regeneration in their lower portions only. The bony defects filled with particulate dentin-plaster of Paris and PRP material showed complete healing and there was no space found between the implant surface and new bone.

(Rodriguez, Anastassov, Lee, Buchbinder, & Wettan, 2003) investigated the clinical applicability of using deproteinated bovine bone mixed with autologous platelet rich plasma (PRP) in human maxillary sinus augmentations in severely resorbed posterior maxillary alveolar processes with simultaneous insertion of endosseous dental implants. The use of platelet rich plasma in combination with deproteinated bovine bone is effective for maxillary sinus augmentation with simultaneous insertion of endosseous dental implants in severely resorbed posterior maxillae. The bone biopsy from the patients showed evidence of viable new bone formation in close approximation to the xenograft. The bone density of the grafted bone was similar or exceeded the bone density of the surrounding native maxillary bone.

(Lekovic et al., 2003) in their study on effectiveness of a combination of platelet-rich plasma, bovine porous bone mineral and guided tissue regeneration in the treatment of mandibular grade II molar furcations in humans, the combination has been shown to be an effective modality of periodontal regenerative therapy for intrabony defects as revealed by gain in clinical attachment and defect fill. Control sites were treated exactly the same as experimental sites, except for the

application of PRP, BPBM or the collagen membrane for GTR. The results showed that the experimental group presented with significantly greater pocket reduction, gains in clinical attachment, vertical defect fill, and horizontal defect fill than the control group.

(Mazor, Peleg, Garg, & Luboshitz, 2004) performed a study on 105 patients who required sinus augmentation with crestal bone height of less than 5 mm in the posterior maxilla. A composite bone graft that consisted of 30% to 40% autogenous bone harvested from the lateral wall of the maxilla, zygomatic–maxillary buttress and the tuberosity and 60% to 70% xenograft. All sinus augmentations were carried out simultaneously with dental implants. Their previous results with the sinus–lift procedure before applying PRP show that the average exposure time was more than 9 months. In this study, applying PRP reduced the time period to exposure by an average of 3 months.

(Eppley, Woodell, & Higgins, 2004) in their study, to accurately count platelet numbers, and to determine whether platelet activation occurs during platelet-rich plasma preparation, and quantitate growth factors released from the platelets from a commercially available platelet concentration preparation system found an 8-fold increase in platelet concentration in platelet-rich plasma compared with that of whole blood (baseline whole blood, 197 ± 42 × 103 platelets/μl; platelet concentrate, 1600 ± 330 × 103 platelets/μl). The concentration of growth factors also increased with increasing platelet number. However, growth factor concentration varied from patient to patient, and a variety of potentially therapeutic growth factors were detected and released from the platelets in significant levels in platelet-rich plasma preparations. Sufficient concentrates and release of these growth factors through autologous platelet gels may be capable of

expediting wound healing in a variety of as yet undetermined specific wound applications.

(Sammartino et al., 2005) analyzed the effects of autologous PRP on periodontal tissues after the extraction of the third molar. They showed that PRP is effective in inducing and accelerating bone regeneration for the treatment of periodontal defects at the distal root of the mandibular second molar after surgical extraction of a mesioangular, deeply impacted mandibular third molar, because of the decrease in both PD and the attachment gain.

(Kanno, Takahashi, Tsujisawa, Ariyoshi, & Nishihara, 2005), studied on Human osteosarcoma cell lines HOS and SaOS-2 , PRP prepared from freshly drawn human venous blood containing a large number of platelets was used to enhance the viability of HOS and SaOS-2 cells in a dose-dependent manner . The MTT assay was used to examine the effects of PRP on osteoblast viability. Evaluation of the growth and differentiation, alkaline phosphatase activity was assessed and the expression of procollagen type I, osteopontin, and osteoprotegerin mRNA was measured using semiquantitative reverse transcriptase-polymerase chain reaction. The results suggest that PRP has a favorable effect on human osteoblast-like cells, and acts both to enhance bone regeneration and also as an activator in wound healing.

(Kassolis & Reynolds, 2005) in his study on ten patients who underwent bilateral maxillary subantral sinus augmentation, with sites within subjects randomized to receive FDBA plus PRP or FDBA plus membrane, the histomorphometric analysis revealed a significantly higher percentage of vital tissue in sinuses after treatment with FDBA and PRP than with FDBA and membrane. Moreover, the percentage of bone formation in sinuses augmented

with the combination of FDBA plus PRP was nonsignificantly (P <= 0.10) higher than in sinuses grafted with FDBA plus membrane. Residual graft particles constituted a significantly higher percentage of the regenerate in sinuses treated with FDBA plus membrane than in sinuses augmented with FDBA plus PRP. Grafts sites augmented with PRP were associated with a consistently and significantly higher ratio of vital bone to graft particles compared with contralateral sites grafted with FDBA alone.

(Landesberg, Roy, & Glickman, 2000) proposes an alternative preparation method of platelet-rich plasma (PRP). They compared the use of thrombin receptor agonist peptide-6 (TRAP) and bovine thrombin as a clotting agent in the preparation of PRP. PRP was prepared by centrifugation and clotted with thrombin or TRAP. TRAP/ Allogro, TRAP/ BioOss, and TRAP/ BioGlass all exhibited minimal retraction. The use of TRAP to activate clot formation in the preparation of PRP may be safe alternative to bovine thrombin. It results in an excellent working time and significantly less clot retraction than the currently available methods of PRP production.

(Graziani, Ducci, & Tonelli, 2005) observed on six patients (age range, 29–58) undergoing sinus augmentation with intraoral bone grafts, platelet-rich plasma, and cryoprecipitate, the amount of bone regeneration, which was evaluated quantitatively and qualitatively with Spiral CT (Dentascan) pre-and postoperatively 6 months after the intervention. Orthopantomography was performed preoperatively 3 and 6 months after the surgery. Orthopantomography indicated mineralization as early as 3 months postoperatively in the entire study population. This technique appeared to be safe and effective. Bone density was evaluated on the Dentascan with the Hounsfield-Misch classification. The

radiological results confirmed the efficiency of the osteoplatelet gel to accelerate and increase the formation and maturation of bone.

(Oyama, Nishimoto, & Takeda, 2005) performed alveolar bone grating utilizing PCBM incorporated with platelet-rich plasma (PRP) and obtained better results in quantitative evaluation of regenerated bone than PCBM grafting. They extracted PRP from bone marrow aspirate (BMA) instead of peripheral blood and undertook secondary alveolar bone grafting with beta-tricalcium phosphate (b-TCP) and PRP from BMA concentrating not only platelets, but also stem cells from BMA, by simple and cost-effective technique. Computed-tomogram taken 6 months after the operation showed sufficient osseo-regeneration.

According to a comparative study by **(Vivek & Sripathi Rao, 2009)** to evaluate osseous regeneration potential of platelet rich plasma for bone blending and trabecular bone formation, healing started earlier in PRP site compared to control, non PRP site. The study showed that autologous PRP is biocompatible and has significantly improved soft tissue healing, bone regeneration and increase in bone density in extraction sockets.

(Shivashankar, Johns, Vidyanath, & Sam, 2013) in their case report combined graft material [platelet rich fibrin (PRF) and hydroxyapatite (HA)] and barrier membrane to treat a large periapical lesion. Based on the results, they hypothesized that the use of PRF in conjunction with HA crystals might have accelerated the resorption of the graft crystals and would have induced the rapid rate of bone formation.

(Hiremath, Motiwala, Jain, & Kulkarni, 2014) in their study observed that repair and regeneration of a large periapical lesion was achieved by using a

combination of growth factors and HA bone graft. Healing was observed within 8 months which were confirmed by CT, following improved bone density.

(Eldibany & Shokry, 2014) conducted a study on 15 patients with large mandibular odontogenic cysts which were treated by enucleation, and grafting of bone defects by a combination of Nanobone and PRF. Accelerated wound healing was observed in all cases without any signs of post-operative complications. On the 9^{th} month post-operatively the surface area decreased by 51% and there was an increase of 50.8% in bone density.

(Baslarli, Tumer, Ugur, & Vatankulu, 2015) observed that the average increase in technetium-99m methylene diphosphonate uptake as an indication of enhanced bone healing did not differ significantly between PRF-treated and non-PRF-treated sockets 30 and 90 days postoperatively. Thus, concluding that PRF might not lead to enhanced bone healing in impacted mandibular third molar extraction sockets 30 and 90 days after surgery.

SURGICAL ANATOMY

MANDIBULAR THIRD MOLAR

The mandible consists of a horseshoe shaped body and two flat, broad rami. Each ramus is surmounted by two processes, viz. coronoid process and condylar process.

The lower third molar tooth is situated at the distal end of the body of the mandible where it meets a relatively thin ramus.

This meeting point constitutes a line of weakness and a fracture may occur if undue force is exerted during elevation of impacted third molar. The tooth is embedded between the thick buccal alveolar bone and a thin lingual cortical plate. When the mandible is viewed from below, it will be seen that the wisdom tooth socket lies on a prominent ledge or shelf of lingual bone. In many instances the lingual bone consists of a thin cortical plate less than 1 mm in thickness.

The buccal bone is predominantly formed by the buccal cortical plate of mandible and the external oblique ridge, the latter being the site of insertion of buccinator muscle. Reduction of the buccal plate will not permit the same ease of surgical access and its loss tends to weaken the mandible. The external oblique ridge is a bulky prominence and it impedes the buccal surgical approach to the wisdom tooth.

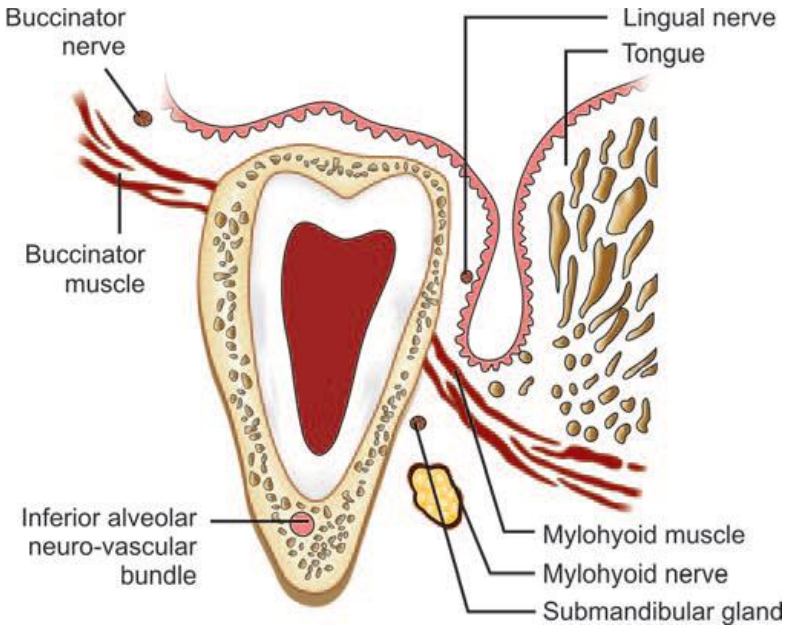


Figure 1: Schematic diagram showing coronal section through the third molar region and the relationship of important anatomical structures to impacted mandibular third molar

Neurovascular Bundle

Below or alongside the roots of the third molar is the mandibular canal. The canal is usually positioned apically and slightly buccal to the third molar roots. The canal encloses the neurovascular bundle. The neurovascular bundle contains the inferior alveolar artery, vein and nerve enclosed in a fascial sheath. Since the calcification of the mandibular canal is completed before formation of the roots of third molar, the growing roots may impinge on the canal causing its deflection.

Occasionally roots are indented by the mandibular canal, and rarely penetration of the roots of the wisdom tooth by this structure may occur. In the latter case, the neurovascular bundle will be torn during extraction of the tooth. Sometimes the apices may reach the superior wall of the canal and protrude into it.

From its start at the mandibular foramen, the canal and its contents are surrounded by a thin layer of bone with a configuration similar to lamina dura and this is radiographically detectable. In cases where the roots of the third molar are in direct contact with the neurovascular bundle, the lamina dura may be partially or totally absent.

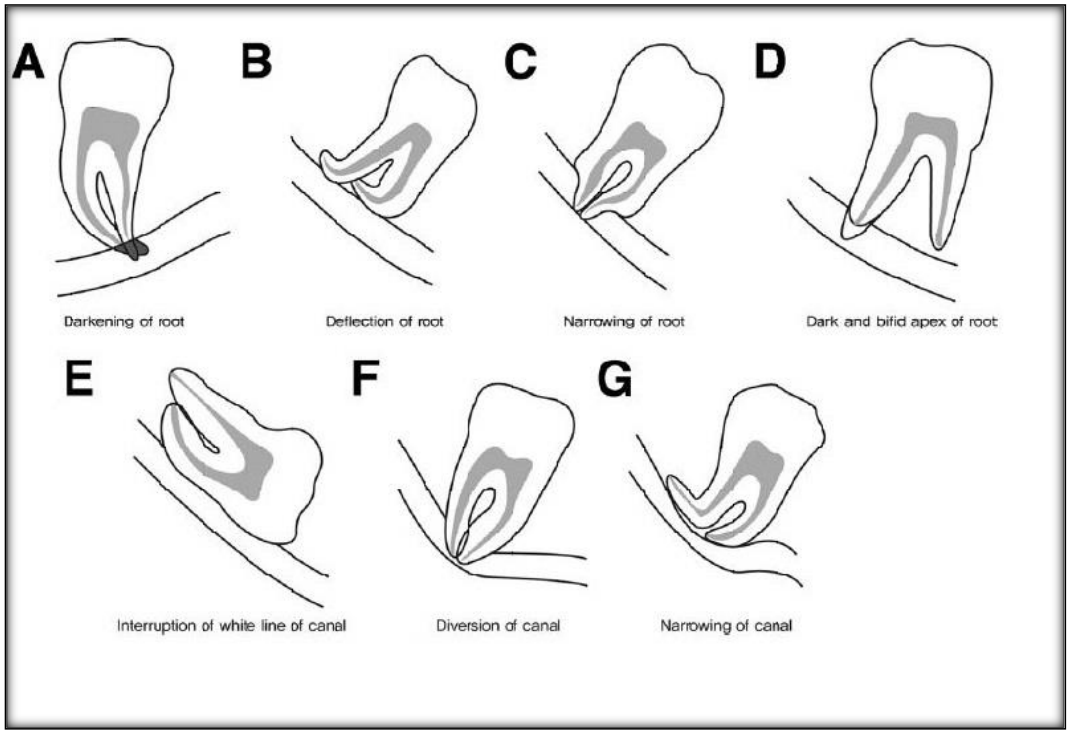


Figure 2: Rood's Radiographic Predictors of Potential Tooth Proximity to the Inferior Alveolar Canal (Rood JP, Shehab BA. The radiological prediction of inferior alveolar nerve injury during third molar surgery. Br J Oral Maxillofac Surg. 1990; 28:20-5)

Retromolar Triangle

Behind the third molar is a depressed roughened area which is bounded by the lingual and buccal crests of alveolar ridge; the retromolar triangle. Lying lateral

to the retromolar triangle is a shallow depression, the retromolar fossa. Either in the retromolar triangle or in the fossa an opening may be present through which emerge branches of the mandibular vessel. This branch supplies the temporalis tendon, buccinator muscle and adjacent alveolus.

The retromolar pad, which is the soft tissue covering the retromolar area is predominantly made up of loose connective tissue.

The tendinous insertion of temporalis muscle terminates as two limiting prongs on the borders of the retromolar triangle.

Facial Artery and Vein

The facial artery and anterior facial vein cross the inferior border of the mandible just anterior to the masseter muscle and have a close relationship to the second and third molar.

Lingual Nerve

The lingual nerve lies on the medial aspect of the third molar. Frequently lingual nerve courses submucosally in contact with the periosteum covering the lingual wall of the third molar socket or it may run below and behind the tooth. The proximity of this important nerve to the third molar places it in danger during the surgical removal of wisdom tooth. Injury to lingual nerve will lead to prolonged anesthesia of the anterior two-thirds of the tongue.

Mylohyoid Nerve

This nerve leaves the inferior alveolar nerve just before the latter enters the mandibular foramen. It then penetrates the spheno-mandibular ligament and

proceeds close to the mandible in the mylohyoid groove. In 16% of the cases the nerve may be enclosed in a canal.

The nerve may be damaged during lingual approach for the removal of impacted mandibular third molar.

Long Buccal Nerve

This nerve emerges through the buccinator muscle and then passes anteriorly on its outer surface. When the mouth is wide open, the level at which the nerve passes through the muscle corresponds to the upper part of the retromolar fossa.

Rarely injury to the nerve can occur when the posterior part of the incision is placed too laterally. This results in anesthesia of the lower part of the buccal mucosa in the molar region.

Musculature

The various muscles surrounding the third molar region are:

• Buccinator - anteriorly

• Temporalis - distally

• Masseter - laterally

• Medial pterygoid and mylohyoid - medially

Buccinator muscle: This horseshoe-shaped muscle forms the musculature of the cheek. It is inserted along the external oblique ridge and continues along the

pterygomandibular raphe. It is attached to the maxilla at the level of the apices of molar roots.

During the surgical removal of deeply impacted third molar, the insertion of attachment of buccinator on the external oblique ridge may have to be severed. This predisposes to marked postoperative swelling, trismus and pain.

Temporalis muscle: This fan-shaped muscle is inserted on the coronoid process and anterior border of mandible. Two tendons can be noticed where the muscle attaches to the anterior border of mandible. The outer tendon is inserted to the anterior border of coronoid process. The inner tendon is attached to the temporal crest of mandible. The retromolar fossa is found in between these tendons.

During buccal approach for the removal of third molars, the outer tendon has to be sectioned to enable reflection of the flap. This in turn will facilitate adequate bone removal from the buccal and distal side.

Masseter: This muscle is inserted into the lateral side of the ramus from the coronoid process up to the angle. The muscle is rarely involved in third molar surgery.

Postoperative edema may extend posteriorly to involve the muscle leading to trismus and pain. Additionally, preoperative or postoperative infection may lead to submasseteric abscess formation.

Medial pterygoid muscle: This is inserted on the medial aspect of mandible in the angle region.

Even though not directly involved in third molar surgery, while using a lingual approach postoperative edema may result in trismus due to secondary involvement of the muscle.

Mylohyoid muscle: This muscle is inserted on the mylohyoid line from canine to the third molar region. In the lingual approach, the insertion of the muscle is partly severed. This leads to transient swallowing difficulty. Moreover, postoperative infection can spread to sublingual or submandibular space.

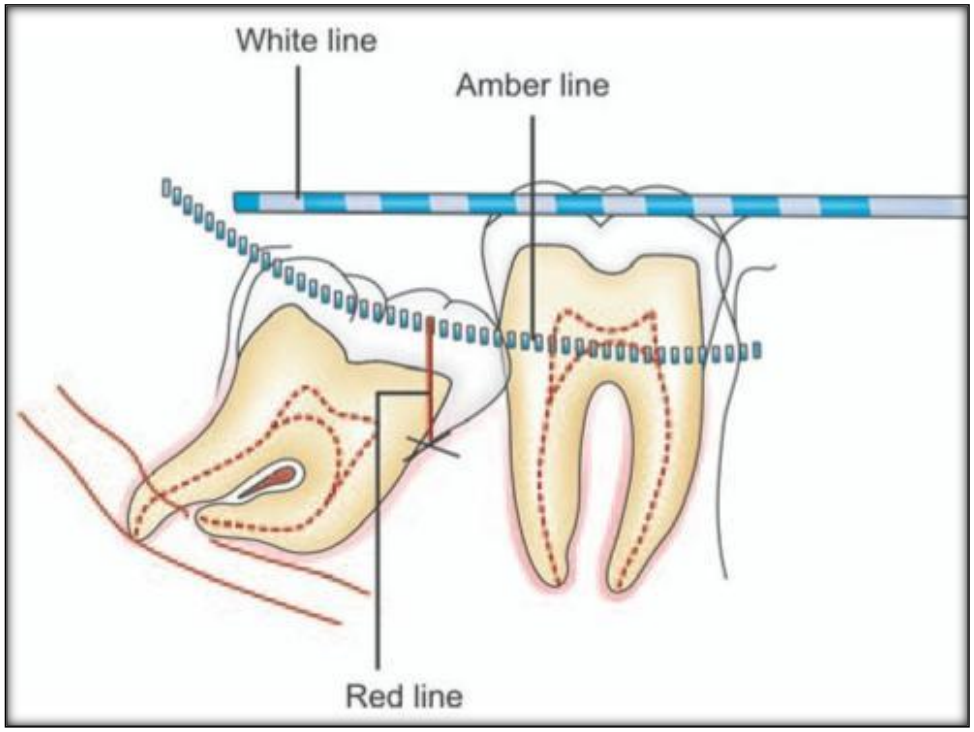


Figure 3: Winter's 'WAR' lines for assessment of difficulty in removal of impacted mandibular third molar

MATERIALS AND METHODS

Selection of Patients

The present study was undertaken at the Department of Oral and Maxillofacial Surgery, Tamil Nadu Government Dental College & Hospital; Chennai, after obtaining approval from the Institutional Ethics Committee (IEC). A total of 30 patients divided into 3 groups; both male and female, aged between 17 and 45 years, who had impacted mandibular third molars with similar anatomical position were randomly selected for this study.

INCLUSION CRITERIA

1. Patients willing for voluntary participation and have signed informed consent.
2. Patients aged between 17-45 years, either sex.
3. Patients with impacted mandibular third molar (38 or 48), with similar anatomical positions, and similar surgical difficulty (Mesioangular impaction).
4. Patients with platelet counts within physiological limits (1.5–4.5 lakhs/cmm).

EXCLUSION CRITERIA

1. Patients with systemic diseases.
2. Patients with possible compromised immune system.
3. Malignant and premalignant conditions.
4. Pregnant women.

5. Patients with documented allergy to any component of the bone substitute or local anesthetics, drugs.
6. Patients unwilling to participate in the study.

SAMPLE SIZE:

- **GROUP I**: a combination of platelet-rich fibrin and hydroxyapatite graft was placed in the post-extraction sockets of 10 patients.
- **GROUP II**: hydroxyapatite graft alone was placed in the post-extraction sockets of 10 patients.
- **GROUP III**: control group of 10 patients with their post-extraction sockets left empty.

STUDY DESIGN

Ethics clearance was obtained from the Institutional ethics committee and the ethical principles were followed throughout the course of the study. Subjects for the study were selected randomly if they satisfied the inclusion criteria with no discrimination on the basis of sex, caste, religion or socioeconomic status. After explaining the study procedure written informed consent in the regional language (Tamil) was obtained from all the subjects selected for the study. Examination was preceded by a thorough medical and dental history of the patients.

STUDY PROTOCOL

- Obtaining medical history and informed consent
- Complete clinical examination by using diagnostic instrument set
- Extra-oral and intra-oral examination
- Pre-operative radiographic evaluation of selected region (OPG)

- Pre surgical preparation
- Surgical procedure
- Post-operative review
- Post-operative care
- Clinical re-evaluation on 1st post-operative day, after 1 week and 2 weeks.
- Radiographic re-evaluation on 1st post-operative day, at the end of 1, 3 and 6 months using OPG, and CT scan at the end of the sixth month.

ARMAMENTARIUM

- Diagnostic instrument set
- Impaction kit
- Micromotor
- Straight handpiece and 703 bur
- Blood collection armamentarium
- Centrifuge
- 10 ml glass test tubes
- Hydroxyapatite graft (G-bone)
- Sterile bowl
- Bone scoop
- Suture material: 3-0 Black Braided Silk

Graft Material

0.5 mg of hydroxyapatite (HA) granules (G-bone) with an average pore size of 0.4-0.9 mm were used in this study.

Preparation of PRF

Requirements:

i. Centrifuge,

ii. 10-ml dry glass test tube (without anticoagulant),

iii. Blood collection armamentarium.

The steps involved are as follows:

a) Blood specimen is collected or drawn from the patient,

b) The blood specimen is placed in the centrifuge and is allowed to spin immediately for 10 minutes at 3000 rpm,

c) Following this the blood sample settles into three layers.

Following layers are formed:

1) The lower fraction containing the RBCs,

2) The middle fraction containing the fibrin clot,

3) The upper fraction containing the straw-colored acellular plasma.

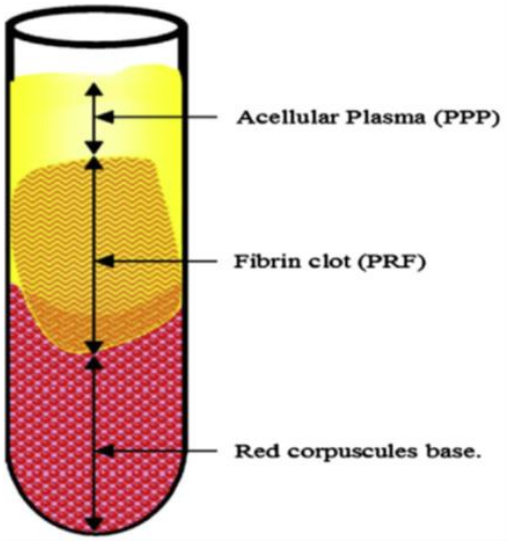


Figure 1: Layers formed after blood centrifugation

- The upper portion of the test tube containing the acellular plasma is removed.
- The middle portion containing the fibrin clot is then removed and is scrapped off from the lower part containing the red blood cells.

Surgical Procedure

Step 1: Transalveolar extraction of mandibular third molars

The procedure was performed with proper aseptic precautions. A single operator carried out all the procedures.

All the patients were advised chlorhexidine mouthwash for oral rinsing before the procedure. Standard scrubbing and painting procedures were done with betadine. Standard draping procedures were followed.

Intra orally inferior alveolar nerve block was given along with lingual and buccal nerve block using 2% Lignocaine with adrenaline 1:80,000. A standard mandibular third molar incision (Ward's incision) was placed distal to second molar continued over the alveolar crest (if the tooth is completely embedded)/ along the buccal gingival sulcus of third molar, upto the distal aspect. Distal releasing incision is started from the distal most point of the third molar across the external oblique ridge into the buccal mucosa.

Anteriorly the incision was extended upto the distal of first molar if needed for better exposure. A full thickness mucoperiosteal flap was raised and the crown of third molar exposed. With the help of a micro motor, straight hand piece and using 703 bur sufficient bone was removed forming a gutter on the mesial, buccal and distal aspects of the tooth. The tooth was elevated with gentle elevation. In

some cases tooth was sectioned and retrieved. The socket was carefully examined for remnants of tissue and then the follicular tissue if present was curetted out from the socket. The socket was irrigated with saline and betadine.

Step 2:

A combination of PRF and hydroxyapatite graft (0.5 gm of porous hydroxyapatite mixed with every 2 ml of PRF) was placed in post-extraction socket of GROUP I patients.

Step 3:

Hydroxyapatite graft (0.5 gm of porous hydroxyapatite) alone was placed in post-extraction socket of GROUP II patients.

Step 4:

Post-extraction socket of GROUP III patients was left empty and served as control.

Step 5:

The wound was closed primarily with 3–0 black braided silk.

Step 6:

Patients were put on an antibiotic course commencing 1 day before surgery to be continued post-operatively for 5 days.

Postoperative Instruction

All the patients were given routine post-operative instructions. They were given Cap. Amoxicillin 500 mg QID, Tab. Metronidazole 400 mg TDS, Tab. Prednisolone 10 mg BID, Tab. Diclofenac 50 mg BID and Tab. Ranitidine 150 mg BID for 5 days.

FOLLOW-UP AND OBSERVATION

All the patients were evaluated:

1. One day prior to the surgery
2. First postoperative day
3. One week postoperatively
4. Two weeks postoperatively
4. One month postoperatively
5. Three months postoperatively
6. Six months postoperatively

- Mouth opening was measured preoperatively and postoperatively using Digital Vernier Caliper.
- The patients were asked to rate the pain intensity on a 10-point Visual Analogue scale (VAS).
- Osseous regeneration was evaluated with the help of standardized orthopantomogram (OPG) taken at 1, 3 and 6 months postoperatively.

  Criteria for radiographic evaluation:

  1. Radiopacity of bone filling the socket.
  2. Presence of trabecular bone formation.

- Bone density was evaluated using computerized tomographic (CT) scan taken at the end of 6 months.

CT scan technique and exposure:

Mandibles were scanned using 16 slice CT, specifics of which were as follows:

Image size: 512 X 512 pixels;

Scanner slice thickness: 0.75 mm;

Exposure time: 26.68 sec and

Field of view: 200 mm.

Images were taken in uncompressed DICOM 3.0 format.

Data analysis:

The data was analysed using SPSS (software package for social sciences) version 20.

First part of the analysis was descriptive analysis of the parameters of age and gender. Pre-op and post-op mouth opening and pain score in the three groups were evaluated using one-way ANOVA analysis. Trabecular pattern assessment was done using chi-square test. Bone density was evaluated after 6 months using one-way ANOVA test.

Figure 1: ARMAMENTARIUM

Figure 2: DIGITAL VERNIER CALIPER

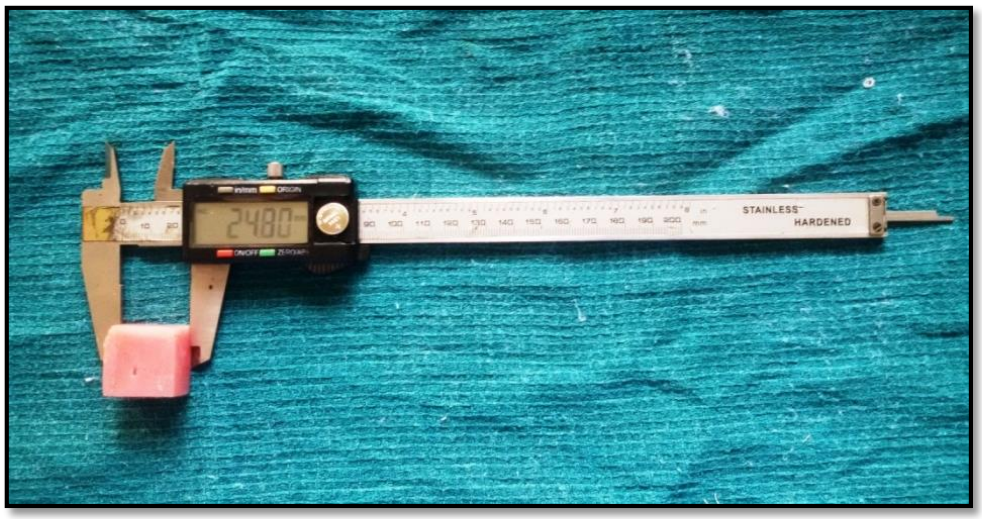


Figure 3: CENTRIFUGE

SURGICAL PROCEDURE

Step 1: INJECTION OF LOCAL ANESTHESIA

Step 2: WARD'S INCISION

Step 3: MUCOPERIOSTEAL FLAP ELEVATION

Step 4: BONE REMOVAL USING MICROMOTOR AND HANDPIECE

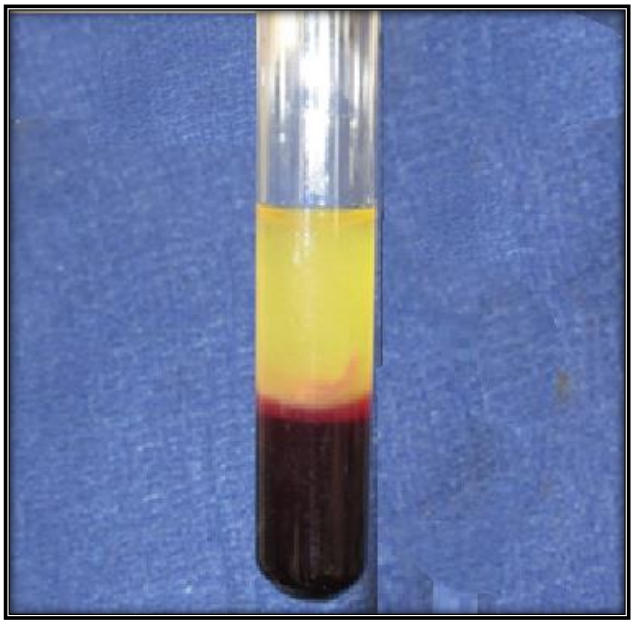
Step 5: ELEVATION OF MANDIBULAR THIRD MOLAR USING STRAIGHT ELEVATOR

Step 6: POST-EXTRACTION SOCKET

GROUP I

Step 7: WITHDRAWAL OF BLOOD FROM BRACHIAL VEIN

Step 8: LAYERS FORMED AFTER CENTRIFUGATION OF BLOOD SAMPLE



Step 9: PLATELET-RICH FIBRIN AND HYDROXYAPATITE GRANULES

Step 10: PRF MIXED WITH HYDROXYAPATITE

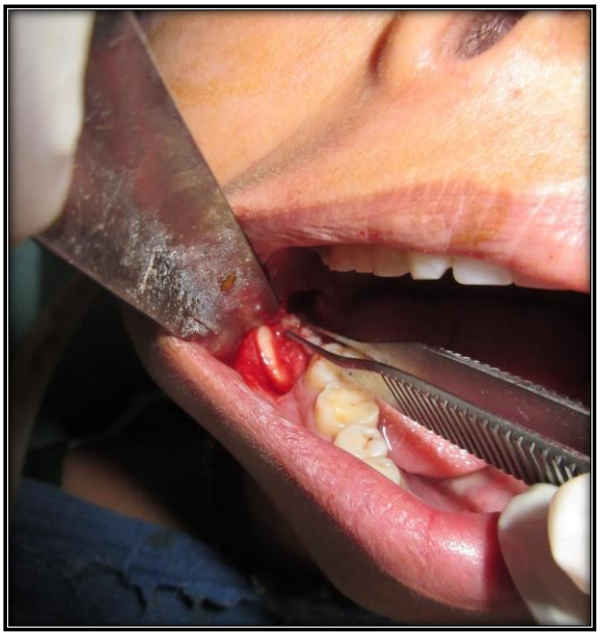
Step 11: PLACEMENT OF PRF AND HA MIXTURE IN POST-EXTRACTION SOCKET OF GROUP I PATIENT

Step 12: PRIMARY CLOSURE USING 3-0 BLACK SILK

GROUP II

Step 13: HYDROXYAPATITE (HA) GRANULES

Step 14: PLACEMENT OF HA GRANULES IN POST-EXTRACTION SOCKET OF GROUP II PATIENT



Step 15: PRIMARY CLOSURE USING 3-0 BLACK SILK

GROUP III

Step 16: EMPTY POST-EXTRACTION SOCKET OF GROUP III PATIENT

Step 17: PRIMARY CLOSURE USING 3-0 BLACK SILK

CASE REPORTS

GROUP I

CASE REPORT 1

NAME **:** Mr. Lional Joshua

AGE/SEX **:** 22 years/ Male

CHIEF COMPLAINT **:** Pain in the left lower back tooth region

HISTORY OF PRESENTING ILLNESS **:** Intermittent pain present in left lower back tooth for past six months which increased in intensity in the last one week

PAST MEDICAL HISTORY **:** Non contributory

PAST SURGICAL HISTORY **:** Non contributory

PAST DENTAL HISTORY **:** Non contributory

GENERAL EXAMINATION **:** 1) Patient is moderately built and nourished

2) Patient is conscious, alert, oriented

3) No signs of pallor, icterus, cyanosis, clubbing, edema and regional lymphadenopathy

LOCAL EXAMINATION

INTRA-ORAL EXAMINATION **:** 1) Mouth opening- 50 mm

2) Impacted- 38, 48

3) Dental caries- 37

4) Missing- 36

INVESTIGATION

OPG **:** Impacted 38, 48

DIAGNOSIS **:** Impaction 38, 48

TREATMENT PLAN **:** Transalveolar extraction of 38 under local anesthesia followed by PRF with Hydroxyapatite graft placement

GROUP I

CASE 1

Figure 1: PRE-OPERATIVE FRONTAL VIEW

Figure 2: POST-EXTRACTION SOCKET

Figure 3: WITHDRAWAL OF BLOOD FROM BRACHIAL VEIN

Figure 4: LAYERS FORMED AFTER CENTRIFUGATION OF BLOOD SAMPLE

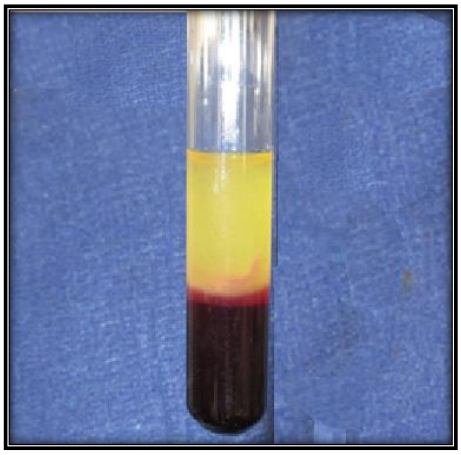


Figure 5: PLATELET-RICH FIBRIN AND HYDROXYAPATITE GRANULES

Figure 6: PRF MIXED WITH HYDROXYAPATITE

Figure 7: PLACEMENT OF PRF AND HA MIXTURE IN POST-EXTRACTION SOCKET

Figure 8: PRIMARY CLOSURE USING 3-0 BLACK SILK

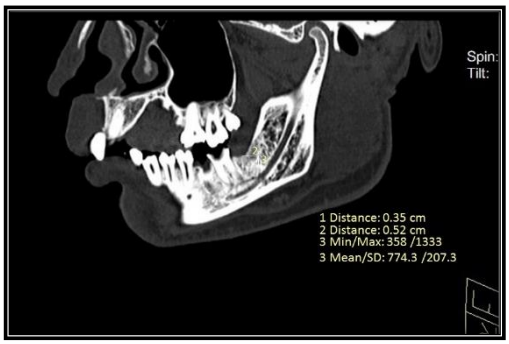
Figure 9: PRE-OPERATIVE OPG

Figure 10: IMMEDIATE POST-OPERATIVE OPG

Figure 11: 6-month post-op OPG

Figure 12: CT SCAN AT THE END OF SIX MONTHS

(Mean Bone Density- 774.3 HU)



CASE REPORT 2

NAME **:** Mrs. Rooth

AGE/SEX **:** 32 years/ Female

CHIEF COMPLAINT **:** Pain in the left lower back tooth region

HISTORY OF PRESENTING ILLNESS : Pain present in left lower back tooth for past three days

PAST MEDICAL HISTORY **:** Non contributory

PAST SURGICAL HISTORY **:** Non contributory

PAST DENTAL HISTORY **:** Non contributory

GENERAL EXAMINATION **:** 1) Patient is moderately built and nourished
2) Patient is conscious, alert, oriented
3) No signs of pallor, icterus, cyanosis, clubbing, edema and regional lymphadenopathy

LOCAL EXAMINATION

INTRA-ORAL EXAMINATION **:** 1) Mouth opening- 33 mm
2) Impacted- 38
3) Filled- 36, 37

4) RCT treated- 11, 21, 22

5) Missing- 14, 16, 25, 46

INVESTIGATION

OPG **:** Impacted 38

DIAGNOSIS **:** Impaction 38

TREATMENT PLAN **:** Transalveolar extraction of 38 under local anesthesia followed by PRF with Hydroxyapatite graft placement

CASE 2

Figure 1: PRE-OPERATIVE FRONTAL VIEW

Figure 2: PRE-OPERATIVE OPG

Figure 3: IMMEDIATE POST-OPERATIVE OPG

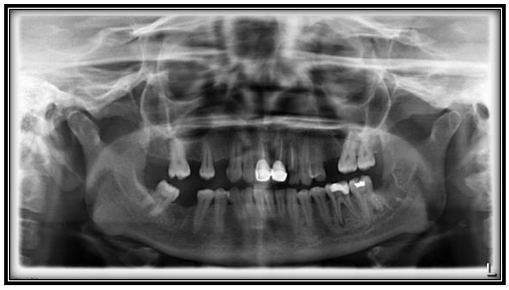


Figure 4: 6-MONTH POST-OP OPG

CASE REPORT 3

NAME **:** Mrs. Ananthi

AGE/SEX **:** 29 years/ Female

CHIEF COMPLAINT **:** Pain in the right lower back tooth region

HISTORY OF PRESENTING ILLNESS **:** Intermittent pain present in right lower back tooth for past one month which increased in intensity in the last one week

PAST MEDICAL HISTORY **:** Non contributory

PAST SURGICAL HISTORY **:** Non contributory

PAST DENTAL HISTORY **:** Non contributory

GENERAL EXAMINATION **:** 1) Patient is moderately built and nourished
2) Patient is conscious, alert, oriented
3) No signs of pallor, icterus, cyanosis, clubbing, edema and regional lymphadenopathy

LOCAL EXAMINATION

INTRA-ORAL EXAMINATION **:** 1) Mouth opening- 26 mm
2) Impacted- 48

INVESTIGATION

OPG **:** Impacted 48

DIAGNOSIS **:** Impaction 48

TREATMENT PLAN **:** Transalveolar extraction of 48 under local anesthesia followed by PRF with Hydroxyapatite graft placement

CASE 3

Figure 1: PRE-OPERATIVE FRONTAL VIEW

Figure 2: PRE-OPERATIVE OPG

Figure 3: IMMEDIATE POST-OPERATIVE OPG

Figure 4: 6-MONTH POST-OP OPG

CASE REPORT 4

NAME **:** Mrs. Sangeetha

AGE/SEX **:** 26 years/ Female

CHIEF COMPLAINT **:** Pain in the right lower back tooth region

HISTORY OF PRESENTING ILLNESS **:** Intermittent pain present in right lower back tooth for past one month which increased in intensity in the last two days

PAST MEDICAL HISTORY **:** Non contributory

PAST SURGICAL HISTORY **:** Non contributory

PAST DENTAL HISTORY **:** Non contributory

GENERAL EXAMINATION **:** 1) Patient is moderately built and nourished
2) Patient is conscious, alert, oriented
3) No signs of pallor, icterus, cyanosis, clubbing, edema and regional lymphadenopathy

LOCAL EXAMINATION

INTRA-ORAL EXAMINATION **:** 1) Mouth opening- 32 mm
2) Dental caries- 36

3) Impacted- 18, 38, 48

INVESTIGATION

OPG **:** Impacted 18, 38, 48

DIAGNOSIS **:** Impaction 18, 38, 48

TREATMENT PLAN **:** Transalveolar extraction of 48 under local anesthesia followed by PRF with Hydroxyapatite graft placement

CASE 4

Figure 1: PRE-OPERATIVE FRONTAL VIEW

Figure 2: PRE-OPERATIVE OPG

Figure 3: IMMEDIATE POST-OPERATIVE OPG

Figure 4: 6-MONTH POST-OP OPG

CASE REPORT 5

NAME **:** Mr. Mohan Raj

AGE/SEX : 40 years/ Male

CHIEF COMPLAINT **:** Pain in the right lower back tooth region

HISTORY OF PRESENTING ILLNESS **:** Pain while eating in the right lower back tooth for past one month

PAST MEDICAL HISTORY **:** Non contributory

PAST SURGICAL HISTORY **:** Non contributory

PAST DENTAL HISTORY **:** Non contributory

GENERAL EXAMINATION **:** 1) Patient is moderately built and nourished
2) Patient is conscious, alert, oriented
3) No signs of pallor, icterus, cyanosis, clubbing, edema and regional lymphadenopathy

LOCAL EXAMINATION

INTRA-ORAL EXAMINATION **:** 1) Mouth opening- 37 mm
2) Missing- 33
3) Impacted- 48

INVESTIGATION

OPG **:** Impacted 48

DIAGNOSIS **:** Impaction 48

TREATMENT PLAN **:** Transalveolar extraction of 48 under local anesthesia followed by PRF with Hydroxyapatite graft placement

CASE 5

Figure 1: PRE-OPERATIVE FRONTAL VIEW

Figure 2: PRE-OPERATIVE OPG

Figure 3: IMMEDIATE POST-OPERATIVE OPG

Figure 4: 6-MONTH POST-OP OPG

GROUP II

CASE REPORT 1

NAME **:** Mr. Suresh Kumar

AGE/SEX **:** 28 years/ Male

CHIEF COMPLAINT **:** Pain in the right lower back tooth region

HISTORY OF PRESENTING ILLNESS **:** Pain present in right lower back tooth for past two months

PAST MEDICAL HISTORY **:** Non contributory

PAST SURGICAL HISTORY **:** Non contributory

PAST DENTAL HISTORY **:** Non contributory

GENERAL EXAMINATION **:** 1) Patient is moderately built and nourished
2) Patient is conscious, alert, oriented
3) No signs of pallor, icterus, cyanosis, clubbing, edema and regional lymphadenopathy

LOCAL EXAMINATION

INTRA-ORAL EXAMINATION **:** 1) Mouth opening- 39 mm
2) Dental caries- 36, 47
3) Impacted- 38, 48

INVESTIGATION

OPG **:** Impacted 38, 48

DIAGNOSIS **:** Impaction 38, 48

TREATMENT PLAN **:** Transalveolar extraction of 48 under local anesthesia followed by hydroxyapatite graft placement

GROUP II

CASE 1

Figure 1: PRE-OPERATIVE FRONTAL VIEW

Figure 2: POST-EXTRACTION SOCKET

Figure 3: HYDROXYAPATITE (HA) GRANULES

Figure 4: PLACEMENT OF HA GRANULES IN POST-EXTRACTION SOCKET

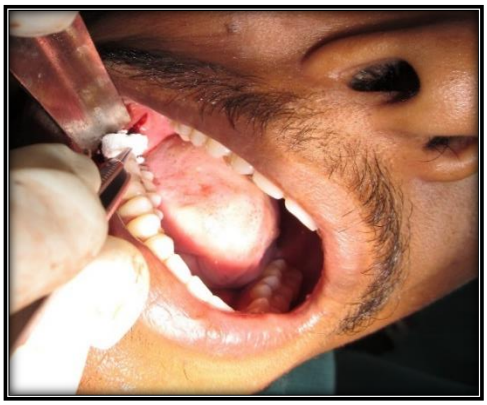


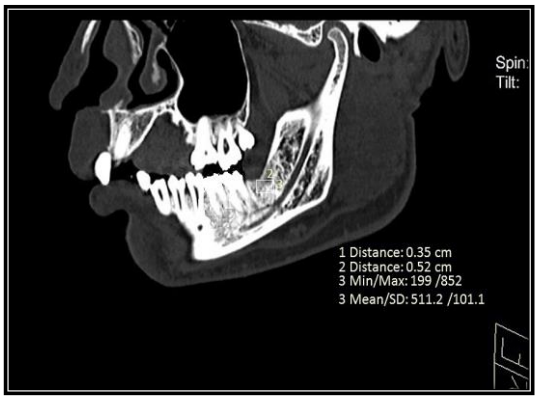
Figure 5: PRIMARY CLOSURE USING 3-0 BLACK SILK

Figure 6: PRE-OPERATIVE OPG

Figure 7: IMMEDIATE POST-OPERATIVE OPG

Figure 8: 6-MONTH POST-OP OPG

Figure 9: CT SCAN AT THE END OF SIX MONTHS (Mean Bone Density- 511.2 HU)



CASE REPORT 2

NAME **:** Mrs. Pushpam

AGE/SEX **:** 45 years/ Female

CHIEF COMPLAINT **:** Pain in the left lower back tooth region

HISTORY OF PRESENTING ILLNESS : Pain present in left lower back tooth for past two months associated with difficulty in mouth opening and eating

PAST MEDICAL HISTORY **:** Non contributory

PAST SURGICAL HISTORY **:** Non contributory

PAST DENTAL HISTORY **:** Non contributory

GENERAL EXAMINATION **:** 1) Patient is moderately built and nourished
2) Patient is conscious, alert, oriented
3) No signs of pallor, icterus, cyanosis, clubbing, edema and regional lymphadenopathy

LOCAL EXAMINATION

INTRA-ORAL EXAMINATION **:** 1) Mouth opening- 28 mm
2) Missing- 16, 36

3) Impacted- 38

INVESTIGATION

OPG **:** Impacted 38

DIAGNOSIS **:** Impaction 38

TREATMENT PLAN **:** Transalveolar extraction of 38 under local anesthesia followed by hydroxyapatite graft placement

CASE 2

Figure 1: PRE-OPERATIVE FRONTAL VIEW

Figure 2: PRE-OPERATIVE OPG

Figure 3: IMMEDIATE POST-OPERATIVE OPG

Figure 4: 6-MONTH POST-OP OPG

CASE REPORT 3

NAME **:** Mrs. Kameshwari

AGE/SEX **:** 37 years/ Female

CHIEF COMPLAINT **:** Pain in the left lower back tooth region

HISTORY OF PRESENTING ILLNESS **:** Pain present in left lower back tooth for the past two weeks

PAST MEDICAL HISTORY **:** Non contributory

PAST SURGICAL HISTORY **:** Non contributory

PAST DENTAL HISTORY **:** Non contributory

GENERAL EXAMINATION **:** 1) Patient is moderately built and nourished
2) Patient is conscious, alert, oriented
3) No signs of pallor, icterus, cyanosis, clubbing, edema and regional lymphadenopathy

LOCAL EXAMINATION

INTRA-ORAL EXAMINATION **:** 1) Mouth opening- 37 mm
2) Impacted- 38, 48

INVESTIGATION

OPG **:** Impacted 38, 48

DIAGNOSIS **:** Impaction 38, 48

TREATMENT PLAN **:** Transalveolar extraction of 38 under local anesthesia followed by hydroxyapatite graft placement

CASE 3

Figure 1: PRE-OPERATIVE FRONTAL VIEW

Figure 2: PRE-OPERATIVE OPG

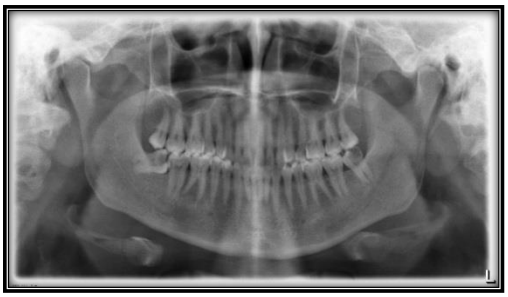


Figure 3: IMMEDIATE POST-OPERATIVE OPG

Figure 4: 6-MONTH POST-OP OPG

CASE REPORT 4

NAME **:** Mrs. Mallika

AGE/SEX **:** 40 years/ Female

CHIEF COMPLAINT **:** Pain in the left lower back tooth region

HISTORY OF PRESENTING ILLNESS **:** Pain present in left lower back tooth for the past four months

PAST MEDICAL HISTORY **:** Non contributory

PAST SURGICAL HISTORY **:** Non contributory

PAST DENTAL HISTORY **:** Non contributory

GENERAL EXAMINATION **:** 1) Patient is moderately built and nourished
2) Patient is conscious, alert, oriented
3) No signs of pallor, icterus, cyanosis, clubbing, edema and regional lymphadenopathy

LOCAL EXAMINATION

INTRA-ORAL EXAMINATION **:** 1) Mouth opening- 29 mm
2) Missing- 16, 21, 26
3) Dental caries- 34
4) Impacted- 38

INVESTIGATION

OPG **:** Impacted 38

DIAGNOSIS **:** Impaction 38

TREATMENT PLAN **:** Transalveolar extraction of 38 under local anesthesia followed by hydroxyapatite graft placement

CASE 4

Figure 1: PRE-OPERATIVE FRONTAL VIEW

Figure 2: PRE-OPERATIVE OPG

Figure 3: IMMEDIATE POST-OPERATIVE OPG

Figure 4: 6-MONTH POST-OP OPG

CASE REPORT 5

NAME **:** Mrs. Revathi

AGE/SEX **:** 24 years/ Female

CHIEF COMPLAINT **:** Pain in the left lower back tooth region

HISTORY OF PRESENTING ILLNESS **:** Intermittent pain present in left lower back tooth for past four months which increased in intensity in the last one week

PAST MEDICAL HISTORY **:** Non contributory

PAST SURGICAL HISTORY **:** Non contributory

PAST DENTAL HISTORY **:** Non contributory

GENERAL EXAMINATION **:** 1) Patient is moderately built and nourished
2) Patient is conscious, alert, oriented
3) No signs of pallor, icterus, cyanosis, clubbing, edema and regional lymphadenopathy

LOCAL EXAMINATION

INTRA-ORAL EXAMINATION **:** 1) Mouth opening- 35 mm
2) Impacted- 38, 48

3) Dental caries- 16

4) Root stumps- 26

5) Filled- 36

INVESTIGATION

OPG **:** Impacted 38, 48

DIAGNOSIS **:** Impaction 38, 48

TREATMENT PLAN **:** Transalveolar extraction of 38 under local anesthesia followed by hydroxyapatite graft placement

CASE 5

Figure 1: PRE-OPERATIVE FRONTAL VIEW

Figure 2: PRE-OPERATIVE OPG

Figure 3: IMMEDIATE POST-OPERATIVE OPG

Figure 4: 6-MONTH POST-OP OPG

GROUP III

CASE REPORT 1

NAME **:** Mrs. Lalitha

AGE/SEX **:** 28 years/ Female

CHIEF COMPLAINT **:** Pain in the right lower back tooth region associated with difficulty in mouth opening

HISTORY OF PRESENTING ILLNESS **:** Pain present in the right lower back tooth for past 3 days aggravated while taking cold foods

PAST MEDICAL HISTORY **:** Non contributory

PAST SURGICAL HISTORY **:** Non contributory

PAST DENTAL HISTORY **:** Non contributory

GENERAL EXAMINATION **:** 1) Patient is moderately built and nourished
2) Patient is conscious, alert, oriented
3) No signs of pallor, icterus, cyanosis, clubbing, edema and regional lymphadenopathy

LOCAL EXAMINATION

INTRA-ORAL EXAMINATION **:** 1) Mouth opening- 22 mm

2) Impacted- 28, 38, 48

3) Root stumps- 25, 46

4) Missing- 36

INVESTIGATION

OPG **:** Impacted 28, 38, 48

DIAGNOSIS **:** Impaction 28, 38, 48

TREATMENT PLAN **:** Transalveolar extraction of 48 under local anesthesia

GROUP III

CASE 1

Figure 1: PRE-OPERATIVE FRONTAL VIEW

Figure 2: EMPTY POST-EXTRACTION SOCKET

Figure 3: PRIMARY CLOSURE USING 3-0 BLACK SILK

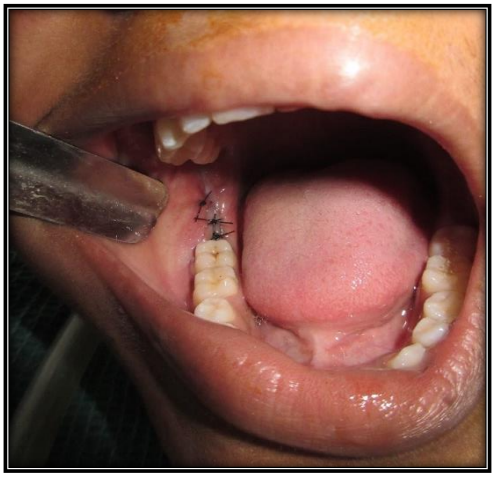


Figure 4: PRE-OPERATIVE OPG

Figure 5: IMMEDIATE POST-OPERATIVE OPG

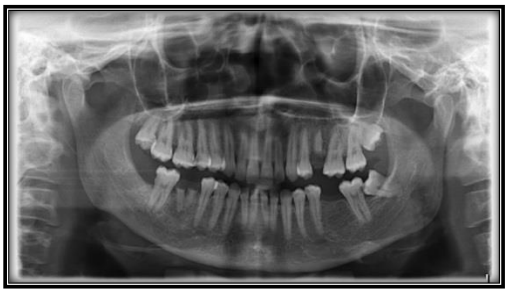
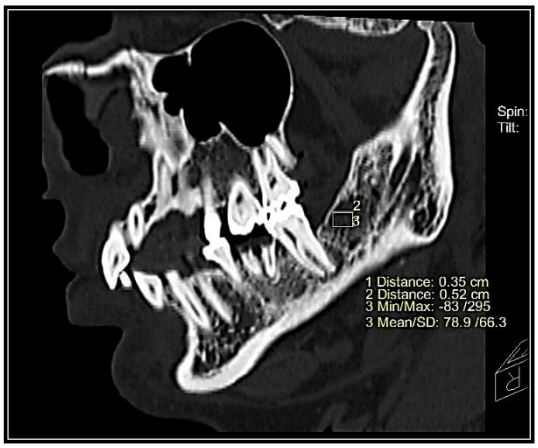


Figure 6: 6-MONTH POST-OP OPG

Figure 7: CT SCAN AT THE END OF SIX MONTHS (Mean Bone Density- 78.9 HU)



CASE REPORT 2

NAME **:** Mr. Suresh

AGE/SEX **:** 38 years/ Male

CHIEF COMPLAINT **:** Pain in the left lower back tooth region

HISTORY OF PRESENTING ILLNESS **:** Intermittent pain present in left lower back tooth for past two weeks which increased in intensity since yesterday

PAST MEDICAL HISTORY **:** Non contributory

PAST SURGICAL HISTORY **:** Non contributory

PAST DENTAL HISTORY **:** Non contributory

GENERAL EXAMINATION **:** 1) Patient is moderately built and nourished
2) Patient is conscious, alert, oriented
3) No signs of pallor, icterus, cyanosis, clubbing, edema and regional lymphadenopathy

LOCAL EXAMINATION

INTRA-ORAL EXAMINATION **:** 1) Mouth opening- 50 mm
2) Impacted- 38

INVESTIGATION

OPG **:** Impacted 38

DIAGNOSIS **:** Impaction 38

TREATMENT PLAN **:** Transalveolar extraction of 38 under local anesthesia

CASE 2

Figure 1: PRE-OPERATIVE FRONTAL VIEW

Figure 2: PRE-OPERATIVE OPG

Figure 3: IMMEDIATE POST-OPERATIVE OPG

Figure 4: 6-MONTH POST-OP OPG

CASE REPORT 3

NAME **:** Mrs. Hemalatha

AGE/SEX **:** 32 years/ Female

CHIEF COMPLAINT **:** Pain in the right lower back tooth region

HISTORY OF PRESENTING ILLNESS **:** Intermittent pain present in both the right and left lower back teeth for past one week

PAST MEDICAL HISTORY **:** Non contributory

PAST SURGICAL HISTORY **:** Non contributory

PAST DENTAL HISTORY **:** Non contributory

GENERAL EXAMINATION **:** 1) Patient is moderately built and nourished
2) Patient is conscious, alert, oriented
3) No signs of pallor, icterus, cyanosis, clubbing, edema and regional lymphadenopathy

LOCAL EXAMINATION

INTRA-ORAL EXAMINATION **:** 1) Mouth opening- 33 mm
2) Impacted- 38, 48

INVESTIGATION

OPG **:** Impacted 38, 48

DIAGNOSIS **:** Impaction 38, 48

TREATMENT PLAN **:** Transalveolar extraction of 48 under local anesthesia

CASE 3

Figure 1: PRE-OPERATIVE FRONTAL VIEW

Figure 2: PRE-OPERATIVE OPG

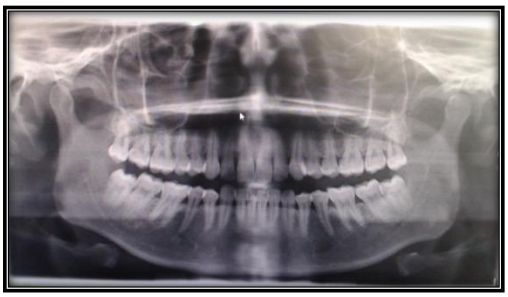


Figure 3: IMMEDIATE POST-OPERATIVE OPG

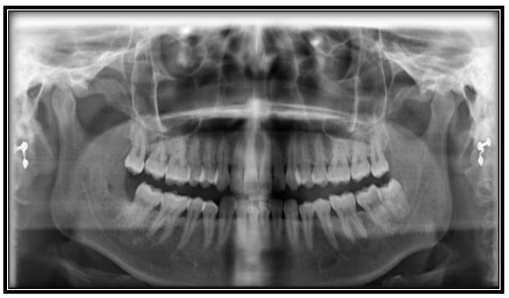


Figure 4: 6-MONTH POST-OP OPG

CASE REPORT 4

NAME **:** Mr. Manivannan

AGE/SEX **:** 24 years/ Male

CHIEF COMPLAINT **:** Pain in the right lower back tooth region

HISTORY OF PRESENTING ILLNESS **:** Intermittent pain present in right lower back tooth for past 2 months which increased in intensity in the last 3 days

PAST MEDICAL HISTORY **:** Non contributory

PAST SURGICAL HISTORY **:** Non contributory

PAST DENTAL HISTORY **:** Non contributory

GENERAL EXAMINATION **:** 1) Patient is moderately built and nourished
2) Patient is conscious, alert, oriented
3) No signs of pallor, icterus, cyanosis, clubbing, edema and regional lymphadenopathy

LOCAL EXAMINATION

INTRA-ORAL EXAMINATION **:** 1) Mouth opening- 53 mm
2) Impacted- 28, 38, 48

INVESTIGATION

OPG **:** Impacted 28, 38, 48

DIAGNOSIS **:** Impaction 28, 38, 48

TREATMENT PLAN **:** Transalveolar extraction of 48 under local anesthesia

CASE 4

Figure 1: PRE-OPERATIVE FRONTAL VIEW

Figure 2: PRE-OPERATIVE OPG

Figure 3: IMMEDIATE POST-OPERATIVE OPG

Figure 4: 6-MONTH POST-OP OPG

CASE REPORT 5

NAME **:** Mr. Selvasundar

AGE/SEX **:** 30 years/ Male

CHIEF COMPLAINT **:** Pain in the right lower back tooth region

HISTORY OF PRESENTING ILLNESS : Pain present in right lower back tooth for past 1 month

PAST MEDICAL HISTORY **:** Non contributory

PAST SURGICAL HISTORY **:** Non contributory

PAST DENTAL HISTORY **:** Non contributory

GENERAL EXAMINATION **:** 1) Patient is moderately built and nourished
2) Patient is conscious, alert, oriented
3) No signs of pallor, icterus, cyanosis, clubbing, edema and regional lymphadenopathy

LOCAL EXAMINATION

INTRA-ORAL EXAMINATION **:** 1) Mouth opening- 41 mm
2) Missing- 24, 36
3) Impacted- 48

INVESTIGATION

OPG **:** Impacted 48

DIAGNOSIS **:** Impaction 48

TREATMENT PLAN **:** Transalveolar extraction of 48 under local anesthesia

CASE 5

Figure 1: PRE-OPERATIVE FRONTAL VIEW

Figure 2: PRE-OPERATIVE OPG

Figure 3: IMMEDIATE POST-OPERATIVE OPG

Figure 4: 6-MONTH POST-OP OPG

OBSERVATION AND RESULTS

This study consisted of a total of 30 patients divided into 3 groups who underwent surgical removal of impacted mandibular third molars, followed by placement of PRF mixed with hydroxyapatite graft in the post-extraction sockets of one group (10 patients), hydroxyapatite graft alone in the second group (10 patients) and the sockets of the third group (10 patients) were left empty.

Group I had 5 male and 5 female patients each, out of which the most common age group was in the range of 21-24 years. In group II there were 3 male and 7 female patients, most common age group range being 37-40 years whereas group III had 4 male and 6 female patients, most of them in the 29-32 year range. The age and sex distribution of the patients is tabulated in Table 1 and graphically represented in Graph 1.

The parameters assessed were:

- Pre-op and post-op mouth opening (in mm)
- Pre-op and post-op pain score (using VAS scale)
- Trabecular pattern assessment and
- Bone density

The mean pre-operative mouth opening in group I was 37 mm, in group II it was 36.2 mm and in group III 36.7 mm. On 1st postoperative day the mean value in group I was 33.3 mm, in group II 32.4 mm and in group III 33 mm. The mean value after 1 week in group I was 38.7, in group II 35.8 mm and in group III it was 36.3

mm. At the end of 2 weeks, the mean mouth opening in groups I, II and III were 39.8 mm, 38.2 mm and 38.1 mm respectively. The observations are tabulated in Table 2.

The mean pre-operative pain score on VAS scale for group I was 5.4, group II was 5 and for group III it was 4.2. The mean value on 1st post-op day was 2.2 for group I, 2.4 for group II and 2.6 for group III. After 1 week the mean values were 1.2, 1.1 and 1.2 for groups I, II and III respectively. At the end of 2 weeks the mean value for all the groups was 1. The observations are tabulated in Table 4.

The trabecular pattern of the bone formed was assessed in an OPG based on the classification proposed by Lindh et al (1996). According to this classification, the trabecular patterns can be classified as alternating dense and sparse, in addition to dense alone, and sparse alone. The PRF with hydroxyapatite site in our study showed 40% of cases with dense trabecular pattern, 50% of cases showed dense sparse and 10% of cases showed sparse pattern in the 1st month. 33.3% of dense pattern, 44.4% of dense sparse, and 22.2% of sparse pattern were seen in the third month. After six months dense pattern was observed in 66.7% of cases and dense sparse pattern in 33.3% of cases.

In the hydroxyapatite site, dense sparse and dense pattern were seen in 40% of cases each whereas 20% cases showed sparse pattern in the 1st month. 30% of dense pattern, 50% of dense sparse, and 20% of sparse pattern were seen in the third month. 37.5% of dense pattern, 50% of dense sparse, and 12.5% of cases showed sparse pattern after six months.

The control group showed 10% cases with dense, 30% with dense sparse and 60% cases with sparse trabecular pattern after 1 month. After 3 months dense pattern was

observed in 11.1% cases, dense sparse and sparse in 44.4% of cases each. 25% cases showed dense, 62.5% dense sparse and 12.5% cases showed sparse trabecular pattern at the end of 6 months. The observations are tabulated in Table 6 and graphically represented in Graph 2.

Bone density was calculated at the end of 6 months using CT scan and the mean values for groups I, II and III were 742 HU, 499 HU and 316 HU respectively. The observations are tabulated in Table 8 and graphically represented in Graph 3.

STATISTICAL ANALYSIS:

Software used: SPSS, Version 20.0

Concept of P value

- If the P value is 0.000 to 0.010 it imply Significant at 1 level (Highly Significant)
- If the P value is 0.011 to 0.050 it imply - Significant at 5 level (Significant)
- If the P value is 0.051 to 1.000 it imply - Not Significant at 5 level (Not Significant)
- If the P value is .000 then put as <0.001.

The mouth opening of the patients was evaluated using one-way ANOVA analysis. At the end of 2 weeks the mean values were 39.8 ± 4.3 mm for group I, 38.2 ± 4.9 mm for group II and 38.1 ± 4.8 mm for group III. P value was 0.667 and the results were not significant. The results are tabulated in Table 3.

The mean pain score on VAS scale evaluated using one-way ANOVA test at the end of 1 week showed values of 1.2 ± 0.4, 1.1 ± 0.3 and 1.2 ± 0.4 for groups I, II and III respectively. The p-value was .804 implying the difference was not significant. After 2 weeks, the mean pain score for all the three groups was 1 and the result was not significant. The results are tabulated in Table 5.

Post-operative trabecular pattern was assessed using chi-square test. The p-value was 0.127 so the difference between the three groups was not significant. The results are tabulated in Table 7.

The bone density at the end of six months was evaluated using one-way ANOVA test. The difference was highly significant with the p-value <0.001. The results are tabulated in Table 9 and Table 10.

OBSERVATION AND RESULTS

GROUP I

Figure 1: Pre-operative OPG

Figure 2: 1-month post-op OPG

Figure 3: 3-months post-op OPG

Figure 4: 6-months post-op OPG

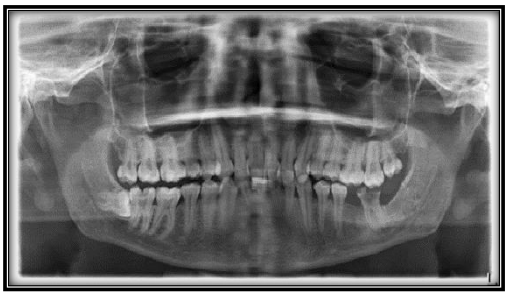
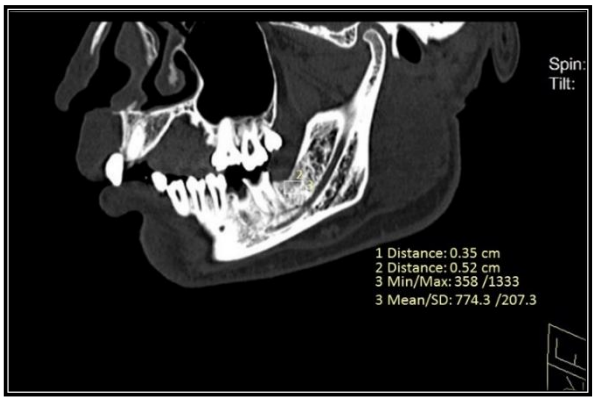


Figure 5: COMPUTERIZED TOMOGRAPHY (CT) SCAN AT THE END OF SIX MONTHS (Mean Bone Density- 774.3 HU)



GROUP II

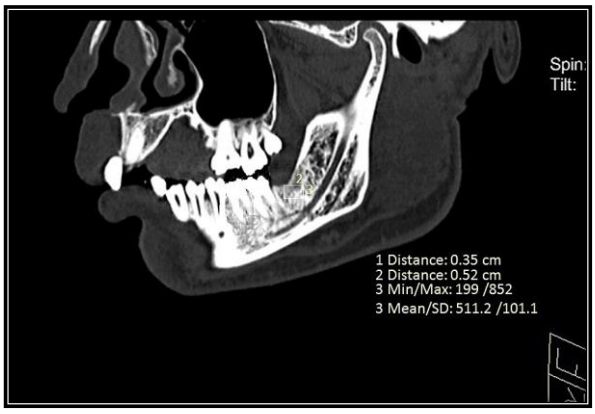
Figure 6: Pre-operative OPG

Figure 7: 1-month post-op OPG

Figure 8: 3-months post-op OPG

Figure 9: 6-months post-op OPG

Figure 10: COMPUTERIZED TOMOGRAPHY (CT) SCAN AT THE END OF SIX MONTHS (Mean Bone Density- 511.2 HU)



GROUP III

Figure 11: Pre-operative OPG

Figure 12: 1-month post-op OPG

Figure 13: 3-months post-op OPG

Figure 14: 6-months post-op OPG

Figure 15: COMPUTERIZED TOMOGRAPHY (CT) SCAN AT THE END OF SIX MONTHS (Mean Bone Density- 78.9 HU)

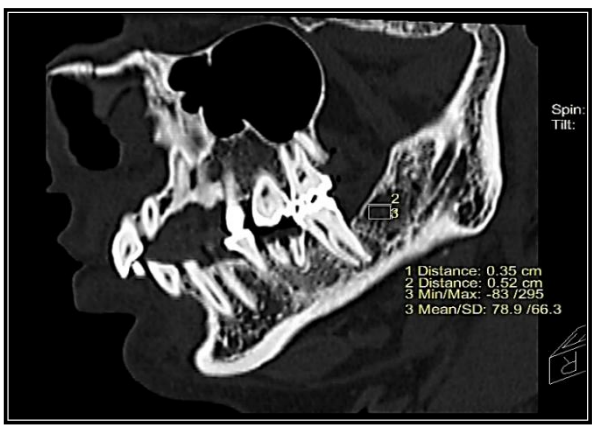
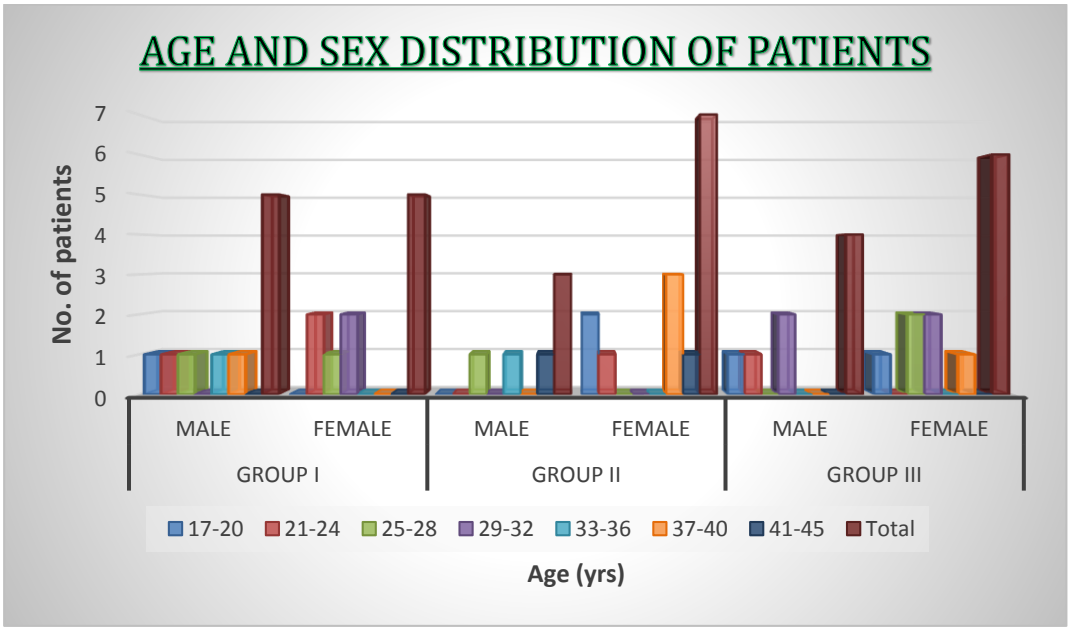


Table 1: Demographic data of the patients included in the study

Age (yrs)	GROUP I		GROUP II		GROUP III	
	Male	**Female**	**Male**	**Female**	**Male**	**Female**
17-20	1	-	-	2	1	1
21-24	1	2	-	1	1	-
25-28	1	1	1	-	-	2
29-32	-	2	-	-	2	2
33-36	1	-	1	-	-	-
37-40	1	-	-	3	-	1
41-45	-	-	1	1	-	-
Total	5	5	3	7	4	6



Graph 1: Bar diagram showing the age and sex distribution of patients

Table 2: Pre-op and post-op mouth opening of the patients in mm

S. No.	Pre-op			Post-op								
	GR I	GR II	GR III	1 DAY			1 WEEK			2 WEEKS		
				GR I	GR II	GR III	GR I	GR II	GR III	GR I	GR II	GR III
1.	50	39	33	41	36	29	49	33	32	51	37	36
2.	37	41	35	33	40	30	37	43	36	41	44	39
3.	32	33	37	28	35	37	39	37	38	38	37	38
4.	33	28	41	25	22	29	34	31	34	36	33	38
5.	37	35	39	36	27	41	37	30	40	39	33	40
6.	43	47	33	39	31	30	42	43	35	40	46	36
7.	39	40	38	35	38	37	37	36	37	38	41	36
8.	26	33	53	30	36	49	38	35	48	38	35	50
9.	35	29	36	32	30	21	35	34	30	36	33	37
10.	38	37	22	34	29	27	39	36	33	41	43	31

Table 3: Mean and standard deviation of the three groups with p values

	Group						P value
	Group I		Group II		Group III		
	Mean	SD	Mean	SD	Mean	SD	
Mouth opening - Pre op	37.00	6.46	36.20	5.81	36.70	7.73	.964
Mouth opening - Post op - 1 day	33.30	4.85	32.40	5.56	33.00	8.04	.949
Mouth opening - Post op - 1 week	38.70	4.24	35.80	4.39	36.30	5.06	.333
Mouth opening - Post op - 2 weeks	39.80	4.32	38.20	4.94	38.10	4.84	.667

Table 4: Pre-op and post-op pain scores of the patients on VAS scale (1-10)

S. No.	Pre-op			Post-op								
	GR I	GR II	GR III	1 DAY			1 WEEK			2 WEEKS		
				GR I	GR II	GR III	GR I	GR II	GR III	GR I	GR II	GR III
1.	1	5	6	3	4	3	2	1	1	1	1	1
2.	4	1	3	2	3	3	1	1	2	1	1	1
3.	5	3	4	1	2	2	1	1	1	1	1	1
4.	2	6	7	2	2	3	1	1	1	1	1	1
5.	7	4	5	3	1	2	1	1	1	1	1	1
6.	5	5	1	2	3	2	1	1	1	1	1	1
7.	8	3	3	2	2	2	1	1	1	1	1	1
8.	7	9	4	2	2	2	2	1	1	1	1	1
9.	6	8	8	3	2	4	1	2	2	1	1	1
10.	9	6	1	2	3	3	1	1	1	1	1	1

Table 5: Mean and standard deviation of the three groups with p values

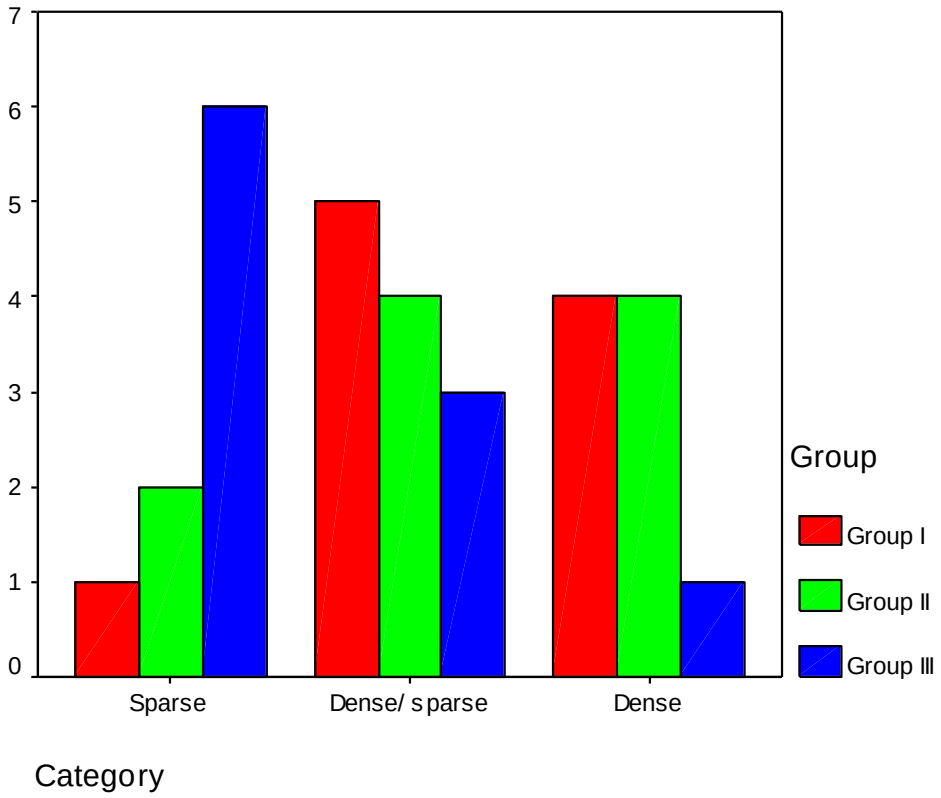
	Group						P value
	Group I		Group II		Group III		
	Mean	SD	Mean	SD	Mean	SD	
Pain score - Pre op	5.40	2.55	5.00	2.40	4.20	2.35	.540
Pain score - Post op - 1 day	2.20	.63	2.40	.84	2.60	.70	.482
Pain score - Post op - 1 week	1.20	.42	1.10	.32	1.20	.42	.804
Pain score - Post op - 2 weeks	1.00	.00	1.00	.00	1.00	.00	-

Table 6: Post-operative trabecular pattern assessment

Catego-ry	1st month			3rd month			6th month		
	Gr I	Gr II	Gr III	Gr I	Gr II	Gr III	Gr I	Gr II	Gr III
Sparse	1	2	6	2	2	4	0	1	1
Dense/ sparse	5	4	3	4	5	4	3	4	5
Dense	4	4	1	3	3	1	6	3	2
Total	10	10	10	9	10	9	9	8	8

Table 7: Category Group Cross tabulation with p-value

			Group			Total	P value
			Gr I	Gr II	Gr III		
Caegory	Sparse	Count	1	2	6	9	.127
		% within Category	11.1%	22.2%	66.7%	100.0%	
		% within Group	10.0%	20.0%	60.0%	30.0%	
	Dense/ sparse	Count	5	4	3	12	
		% within Category	41.7%	33.3%	25.0%	100.0%	
		% within Group	50.0%	40.0%	30.0%	40.0%	
	Dense	Count	4	4	1	9	
		% within Category	44.4%	44.4%	11.1%	100.0%	
		% within Group	40.0%	40.0%	10.0%	30.0%	
Total		Count	10	10	10	30	
		% within Category	33.3%	33.3%	33.3%	100.0%	
		% within Group	100.0%	100.0%	100.0%	100.0%	



Graph 2: Bar diagram showing the post-operative trabecular pattern of the three groups of patients after 1 month, 3 months and 6 months respectively

Table 8: Measure of bone density in Hounsfield units (HU) recorded after 6 months using the computerized tomography (CT) scan

S.No.	GROUP I	GROUP II	GROUP III
1.	523	477	270
2.	922	663	312
3.	487	288	225
4.	717	640	303
5.	800	391	079
6.	813	527	444
7.	1001	511	501
8.	640	498	394
9.	774	-	-
10	-	-	-

Table 9: Mean and standard deviation of the three groups with p values

	Measure of bone density		P value
	Mean	SD	
Group I	741.89	171.14	.000
Group II	499.38	122.11	
Group III	316.00	107.51	

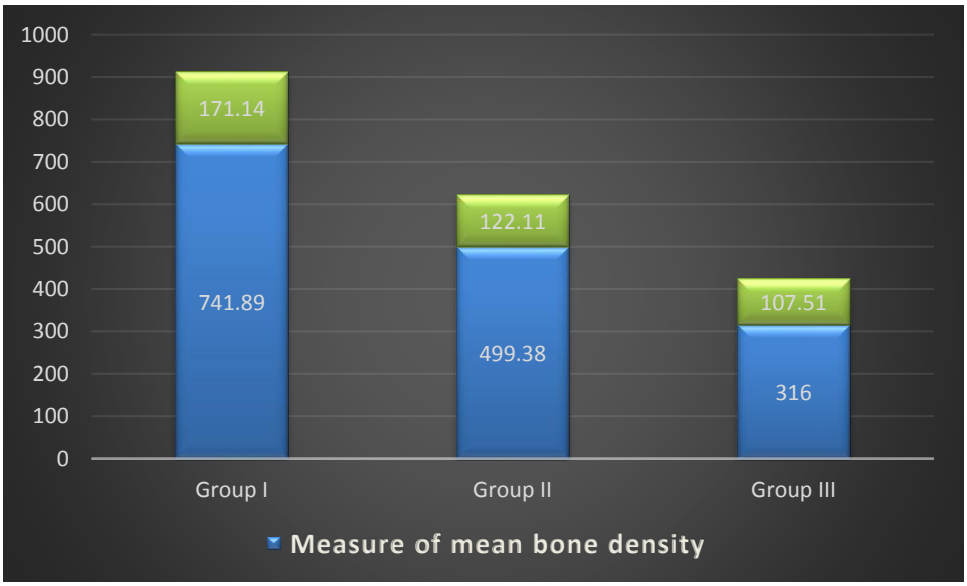
Table 10:

ONE-WAY ANOVA

Measure of bone density

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	777843.236	2	388921.618	20.391	.000
Within Groups	419600.764	22	19072.762		
Total	1197444.000	24			

Graph 3: Bar diagram showing the mean bone density of the three groups of patients



DISCUSSION

The healing of an extraction socket is a complex process involving both tissue repair as well as regeneration. Regeneration by definition is reproduction or reconstitution of a lost or injured part which fully restores the architecture or function of the part. The cellular events responsible for healing are controlled and regulated by specific signaling molecules, growth factors and cytokines. Transforming growth factor β-1 (TGF-beta-1), bone morphogenic protein-2 (BMP-2), and platelet-derived growth factor αβ (PDGF-AB) secreted by cells are recruited to the healing extraction wound in response to stimuli detected at the cell surface[4]. The local availability of these growth factors are enhanced by about threefold or greater in concentration by the addition of autologous platelet rich fibrin.

Ross et al.[48] in 1974 were amongst the pioneers who first described a growth factor from platelets. Growth factors are released after activation from the platelets trapped within fibrin matrix and have been shown to stimulate the mitogenic response in the periosteum for bone repair during normal wound healing. These factors reverse the inhibition of wound healing caused by glucocorticoids, stimulate fibroblast chemotaxis and proliferation and are a potent stimulator of collagen synthesis.

Third molar extractions are often used as a measurement tool for comparing surgical treatments because they are usually performed electively on a younger population that usually do not present with multiple confounding factors (e.g., systemic pathologies, multiple medications). Hence, even in this study third molar extractions have been used to compare three surgical treatment outcomes.

In the present study, noninvasive radiographic techniques were used to arrive at the outcome of the surgical procedures. Even though bone histology studies could have provided additional information, taking into account the invasive nature of the analysis, it was avoided.

Platelet-rich fibrin (PRF) first described by **(Choukroun, Adda, Schoeffler, & Vervelle, 2001)[1]** is a new second generation of platelet concentrate. A simplified processing technique without any complex handling makes it superior to PRP. PRF can be used to promote wound healing, bone regeneration, graft stabilization, wound sealing, and hemostasis. Because the fibrin matrix is better organized, it is able to more efficiently direct stem cell migration and the healing program. Release of growth factors from PRF through in vitro studies and good results from in vivo studies have led to optimize the clinical application of PRF. It was shown that there are better results of PRF over PRP. **(Dohan et al., 2006)[49]** proved a slower release of growth factors from PRF than PRP and observed better healing properties with PRF. It was observed and shown that the cells are able to migrate from fibrin scaffold; while some authors demonstrated the PRF as a supportive matrix for bone morphogenetic protein as well. Taking into consideration these factors, PRF was used in this study.

Alloplasts are biocompatible osteo-conductive materials, used to replace human bone. In this process, vascular tissue invades the graft, bringing with it the osteoblasts that deposit new bone, called ‘creeping substitution’ and represents osteo-conduction (**Barth et al, 1896)[3]**. Both hydroxyapatite (HA) and tricalcium phosphate (TCP) in their ceramic form act as excellent bone graft substitutes in filling bone voids after curettage of benign bone tumors. The alloplastic bone

substitutes when placed in contact with living bone causes no tissue reaction, rapidly consolidates with the host bone and incorporates into the bony framework.

(Deeb et al, 1988)[50] has demonstrated that the porous form of hydroxyapatite allows rapid fibrovascular tissue in-growth and osteoblasts recognize the hydroxyapatite surface which consists of biologic apatite as a bone layer and these cells use that surface for deposition of new bone and may stabilize the graft and help resist micromotion.

For this reason, we chose HA in the present study, so that it could enhance the effects of PRF by maintaining the space for tissue regeneration to occur, as well as by exerting an osteoconductive effect in the bony defect area. Bone grafts alone without a blood clot or angiogenic factors are unlikely to be capable of promoting periapical wound healing **(Butterfield & Bennett, 2005)[51]**. Biologically, a blood clot is a better space filler than all bone grafting materials. A blood clot is the host's own biologic product and is indispensable in tissue wound healing. Tissue wound healing would be impaired without a blood clot, as in a dry socket after tooth extraction.

The present study was undertaken to study the efficacy of platelet-rich fibrin in regeneration of bone when mixed with porous hydroxyapatite and grafted in mandibular third molar socket with that of plain hydroxyapatite (without PRF), with a follow up period of 6 months.

A total of 30 patients were selected for the study, divided into three groups, with 10 patients in each group and were followed up for a period of 6 months. There were 12 male and 18 female patients out of which the most common age group was in the range of 29-32 years. 67% of patients had impacted

right mandibular third molar whereas only 33% of patients had impacted tooth on the left side.

The parameters assessed were:

- Pain and trismus
- Trabecular pattern assessment and
- Bone density

Post-operative trismus was evaluated in all the three groups and the results were not significant statistically.

Pain was also assessed with Visual analog scale (VAS) and it was found that the severity of pain was similar in both study (Group I and Group II) and control (Group III) groups and the results were not significant.

(Ogundipe, Ugboko, & Owotade, 2011)[52] in a prospective randomized comparative clinical study to investigate the effect of PRP gel on postoperative pain, swelling and trismus found that the mean postoperative pain score was lower for the PRP group and was statistically significant. Whereas the figures for swelling and interincisal mouth opening showed the difference was not significant. On the contrary, pain and trismus findings were not significant in our study.

A study by **(Kaur & Maria, 2013)[53]** to evaluate the efficacy of PRP and hydroxyapatite crystals in bone regeneration showed no significant difference in severity of pain between the study and control groups and these results corroborate our findings. Similarly, **(Arenaz-Búa et al., 2010)[54]** found no statistically significant differences between groups regarding pain, swelling,

trismus and infection throughout the postoperative period. Our results were consistent with these findings.

(Lekholm et al, 1985)[55] proposed a classification and established that dense trabeculation and sparse trabeculation were found to be representative imaging features. In an OPG, surrounding cortical bone cannot be visualized as on a cross section, hence trabecular patterns as alternating dense and sparse, in addition to dense alone, and sparse alone were used in this study, as proposed by **(Lindh, Petersson, & Rohlin, 1996)[56].**

Both in Group I and Group II there were 40% of cases each with dense trabecular pattern. On the other hand, 10% in the control group showed dense trabeculation at the end of 1st month. Over a 6 month follow up period 66.7% cases in Group I, 37.5% in Group II and 25% in Group III showed dense pattern.

The dense sparse pattern was seen in 50% of Group I cases, 40% of Group II and 30% Group III by the end of 1st month. After 6 months 33.3% in Group I, 50% in Group II and 62.5% in Group III had dense sparse pattern.

Group I had sparse pattern in 10 % of cases, Group II 20 % and Group III 60% after 1 month whereas at the end of six months 12.5% each in Group II and Group III showed sparse pattern with none of the cases showing sparse pattern in Group I.

(Alissa & Esposito, 2009)[57] investigated the effect of PRP on the healing of hard and soft tissues of extraction sockets and followed up for 3 months. A statistically significant difference with dense homogeneous trabecular pattern was observed. In contrast, the present study found the difference between the three groups to be not significant.

(Anitua et al, 1999)[58] in their study used a true autologous platelet gel to fill the empty alveolae of the patients after tooth extraction and the biopsy specimens (3mm) which were taken 10 to 16 weeks after extraction indicated that both soft and hard tissue healing seemed to be improved but conclusions were not drawn because of no quantitative analysis.

In this study the density of the bone formed in the extraction socket was calculated using CT scan at the end of 6 months. This method used to assess the bone density was based on the suggestion given by **(Diederichs et al, 1996)[59]**. Comparison between the three groups was done using one way ANOVA test. Mean bone density for Group I at the end of six months was 742 ±171 HU; for group II it was 500 ±122 HU and for Group III 316 ±108 HU. The results were found to be highly significant statistically ($p<0.0001$).

(Marx et al, 2004)[60] in their study added PRP to bone grafts, used in mandibular bone defects and evidenced that radiographically the maturation rate was better than that of grafts without platelet-rich plasma. **(Wiltfang et al., 2003)[61]** reported 8% to 10% more bone formation when PRP was added to tricalcium phosphate. **(Antonello et al., 2013)[62]** measured bone density by area histogram analysis and found the result to be statistically significant after a 6-month follow up period.

(Hiremath et al., 2014)[44] and **(Eldibany & Shokry, 2014)[45]** used PRF and hydroxyapatite to manage large periapical inflammatory lesions and reported repair and regeneration occurring within 8 months which was confirmed by CT scan, following improved bone density. The increase in bone density was statistically significant throughout the different follow up periods (9 months).

Even in the present study, the bone density was better in extraction sockets filled with PRF and hydroxyapatite.

(Arenaz-Búa et al., 2010)[54] in their study observed that PRP mixed with other biomaterials facilitates the manipulation of the graft and therefore could be used as a biological carrier in mandibular bone reconstruction but they didn't find statistically significant difference, in contrast to the findings in this study.

The present study showed that PRF has beneficial effects on bone repair, especially when combined with an alloplastic bone substitute, in the early stages of scarring, promoting and accelerating healing events such as mitogenesis, angiogenesis and chemotaxis, corroborating the results obtained by **(Rutkowski, Johnson, Radio, & Fennell, 2010)[63]** who demonstrated significant ($P < 0.0001$) increase in bone density in PRF treated sites compared to control.

(Baslarli et al., 2015)[46] in their findings concluded that PRF might not lead to enhanced bone healing in impacted mandibular third molar extraction sockets 30 and 90 days after surgery, thus differing from the results shown in this study.

This study clearly indicated a definitive improvement in the wound healing and increase in bone density, which signifies and highlights the use of PRF and hydroxyapatite granules, certainly as a valid method in inducing and accelerating bone regeneration. The preparation of PRF is a simple, chair side procedure, safe, cost effective and is made in the preoperative period and demonstrates good results. An added benefit of PRF noted in the present study is its ability to form a biological gel that provides clot stabilization.

The present study was done in extraction sockets with a follow up of 6 months, further clinical trials with a longer duration and in different sites for e.g. in apicoectomy, and other bone defects should be done to get more affirmative and conclusive results.

SUMMARY AND CONCLUSION

Osseous defects repaired using bone grafts has gained importance in dentoalveolar surgery since centuries. After extraction, the surrounding jaw bone tends to recede and atrophy. This atrophy occurs regardless of the patient's age, sex, or teeth. A synthetic bone graft should be placed in the socket to prevent this disuse atrophy.

Socket grafting is the immediate replacement of an extracted tooth with the use of bone grafts, derivates or bone substitutes to promote healing and regeneration, which should be inert chemically, non-carcinogenic, non-inflammatory, non-allergic, dimensionally stable, and resistant to stress.

In the present study, platelet-rich fibrin mixed with hydroxyapatite was used as bone graft material, to enhance the osteoconductive property of hydroxyapatite in mandibular third molar socket.

The benefits of the present study are:

- Since mandibular angle is one of the commonest sites prone to fracture after trauma, a quicker healing response facilitated by using platelet rich fibrin combined with hydroxyapatite will limit the occurrence of any such event in early post-operative period following third molar extraction.
- For orthognathic surgeries like bilateral sagittal split osteotomy (BSSO), the waiting period which is usually 6-9 months after mandibular third molar extraction can be shortened by placing graft material in the extraction socket.

- In patients with hemifacial microsomia, planned for distraction osteogenesis after angular osteotomy, placement of a graft material in the extracted mandibular third molar socket will enable early start of treatment and will give better results.

PRF is an autologous preparation, prepared at the time of surgery which eliminates concerns about disease transmission and immunogenic reactions. It is an investigational biomaterial that demonstrates superior attributes of ease of application, osseointegration and osteoconductance.

The fate of graft materials (hydroxyapatite), when implanted, is different, depending mostly on the rate of resorption and potential for an inflammatory response. The porosity (pore dimension), mechanical properties, crystallinity and fabrication technique of granules also do determine the osteoconductive property of the graft.

The observations in the present study indicate that hydroxyapatite could be successfully used with or without PRF for socket grafting in dentistry. But a faster and better consolidation of graft material and a better osseointegration can be achieved with the addition of PRF in the hydroxyapatite graft material.

Growth factors in general and PRF in particular are part of a new biotechnology with already established efficacy and future potential. It is the responsibility of the clinician to gain a thorough understanding of this biotechnology and to use it correctly and wisely for the benefit of patients.

This study clearly indicated a definitive improvement in the wound healing and increase in bone density, which signifies and highlights the use of PRF combined with hydroxyapatite granules, certainly as a valid method in inducing and accelerating bone regeneration.

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ஒப்புதல் படிவம்
ஆராய்ச்சியின் தலைப்பு

அறுவை சிகிச்சை செய்த கீழ்தாடை ஞானப்பல் குழியில் ஹைட்ராக்சி அப்பட்டைட்டு மற்றும் ஹைட்ராக்சி அப்பட்டைட்டுடன் இரத்த வட்டுகள் நிறைந்த இரத்த உறைதல் மூலப்பொருட்கள்.

பெயர் : புற நோயாளி எண். :

முகவரி : எண் :

தொலைபேசி எண் : வயது/பால் :

நான் ..... வயது ..... என்னுடைய சுயநினைவுடனும் மற்றும் முழு சுதந்திரத்துடனும் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக் கொள்ள ஒப்புதல் அளிக்கிறேன்.

கீழ்காணப்படும் நிபந்தனைகளுக்கு நான் சம்மதிக்கிறேன்.

- நான் இந்த ஆராய்ச்சியின் நோக்கம் மற்றும் ஆராய்ச்சியின் முறைகள் பற்றி முழுமையாக தெரிவிக்கப்பட்டுள்ளேன்.
- இந்த பரிசோதனைக்காக ஞானப்பற்களை அறுவை சிகிச்சை மூலம் எடுக்க வேண்டியுள்ளதாக அறிகிறேன்.
- அறுவை சிகிச்சையின்போது ஹைட்ராக்சி அப்பட்டைட்டு மட்டும் அல்லது ஹைட்ராக்சி அப்பட்டைட்டு மற்றும் இரத்த வட்டுகள் நிறைந்த இரத்த உறைதல் மூலப்பொருள் கொண்டு புதைப்பல் எடுத்த இடத்தில் பொருத்திக் கொள்ள சம்மதிக்கிறேன்.
- என் உடல் பாதிக்கப்பட்டாலோ அல்லது எதிர்பாராத வழக்கத்திற்கு மாறான நோய்குறிகள் தென்பட்டாலோ அதனை விலக்குவதற்கு முழு உரிமை உள்ளதாக அறிக்கிறேன்.
- நான் ஏற்கனவே உட்கொண்ட் மற்றும் உட்கொள்கின்ற மருந்துகளின் விபரங்களை ஆராய்ச்சியாளரிடம் தெரிவித்துள்ளேன்.
- என் மருத்துவ குறிப்பேடுகளை இந்த ஆராய்ச்சியில் பயன்படுத்திக் கொள்ள சம்மதிக்கிறேன்.
- இந்த ஆராய்ச்சி மையமும் ஆராய்ச்சியாளரும் என்னுடைய விபரங்கள் அனைத்தையும் இரகசியமாக வைப்பதாக அறிகிறேன்.

.....	.....	.....
நோயாளியின் பெயர்	கையொப்பம்/கைரேகை	தேதி

.....	.....	.....
ஆராய்ச்சியாளரின் பெயர்	கையொப்பம்	தேதி

Annexure: AF 06/004/01.0

INFORMED CONSENT FORM

STUDY TITLE

"COMPARATIVE EVALUATION OF BONE REGENERATION AFTER SURGICAL REMOVAL OF IMPACTED MANDIBULAR THIRD MOLARS USING HYDROXYAPATITE WITH AND WITHOUT PLATELET RICH FIBRIN"

Participant ID No:

"I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this study and understand that I have the right to withdraw from the study at any time without in any way it affecting my further medical care."

Date	Name of the participant	Signature/thumb impression of the participant

[The literate witness selected by the participant must sign the informed consent form. The witness should not have any relationship with the research team; If the participant doesn't want to disclose his / her participation details to others, in view of respecting the wishes of the participant, he / she can be allowed to waive from the witness procedure (This is applicable to literate participant ONLY). This should be documented by the study staff by getting signature from the prospective participant]

_____

_____

_____

"I have witnessed the accurate reading of the consent form to the potential participant and the individual has had opportunity to ask questions. I confirm that the individual has given consent freely"

Date	Name of the witness	Signature of the witness

Date	Name of the interviewer	Signature of the interviewer

CASE REPORT FORM

COMPARATIVE EVALUATION OF BONE REGENERATION AFTER SURGICAL REMOVAL OF IMPACTED MANDIBULAR THIRD MOLARS USING HYDROXYAPATITE WITH AND WITHOUT PLATELET RICH FIBRIN

Patient's Name : _____

Age/ Sex : _____

Patient's Identification No : _____

Contact Address : _____

_____

_____

Contact No : _____

Institution : TN Govt. Dental College & Hospital,
Chennai - 600 003.

Centre : Dept. of Oral & Maxillofacial Surgery,
TN. Govt. Dental College and Hospital,
Chennai - 600 003

DETAILS OF SURGERY

Procedure followed : Transalveolar extraction of impacted mandibular third molar followed by graft placement

Any other information :

Details of Drug therapy :

POST-OPERATIVE ASSESSMENT:

Parameters assessed:

1. Pain and trismus
2. Assessment of bone trabecular pattern
3. Bone density measurement

Name of the Investigator :

Signature of Investigator :

CASE SHEET PROFORMA

COMPARATIVE EVALUATION OF BONE REGENERATION AFTER SURGICAL REMOVAL OF IMPACTED MANDIBULAR THIRD MOLARS USING HYDROXYAPATITE WITH AND WITHOUT PLATELET RICH FIBRIN

PATIENT'S NAME : _____

AGE/ SEX : _____

PATIENT'S

IDENTIFICATION NO : _____

CONTACT ADDRESS : _____

_____

CONTACT No : _____

INSTITUTION : TN Govt. Dental College & Hospital,
Chennai - 600 003.

CENTRE : Dept. of Oral & Maxillofacial Surgery,
TN. Govt. Dental College and Hospital,
Chennai - 600 003

CHIEF COMPLAINT:

HISTORY OF THE PRESENTING ILLNESS:

CLINICAL FINDINGS:

INVESTIGATIONS:

TREATMENT:

Procedure followed : Transalveolar extraction of impacted mandibular third molar followed by graft placement

FOLLOW UP

1. Pain and trismus
2. Assessment of bone trabecular pattern
3. Bone density measurement

NAME OF THE INVESTIGATOR :

SIGNATURE OF INVESTIGATOR :